# CHAPTER II

# HISTORICAL

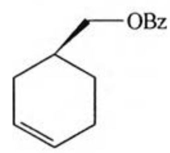
The family Annonaceae belongs to the order Magnoliales (Annonales), which consists of plant families considered the most primitive of angiosperms, including Myristicaceae, Magnoliaceae, Degeneriaceae, Himantandraceae, Canellaceae and Winteraceae. The order Magnoliales itself is allied to more advanced orders such as Laurales (e.g. families Lauraceae and Chloranthaceae), Piperales (e.g. families Piperaceae and Saururaceae), Aristolochiales (e.g. families Aristolochiaceae and Nepenthaceae), Ranunculales (e.g. families Menispermaceae, Ranunculaceae and Berberidaceae) and Papaverales (families Papaveraceae and Fumariacae). In many cases, these phylogenic relationships can be correlated chemotaxonomically.

Studies of the chemical constituents of the Annonaceae revealed various types of compounds, some of which are bioactive secondary metabolites such as polyphenols, essential oils, terpenes, acetogenins, flavonoids, alkaloids, lignans and cyclohexenes. Reviews of cyclohexene derivatives, flavonoids (focusing on chalconoid compounds), and lignans (focusing on 2,5-diaryltetrahydrofuran lignans and 2,3-dihydrobenzofuran neolignans) in the family Annonaceae and related families, together with a review of the annonaceous aporphine alkaloids, particularly the oxoaporphines, dioxoaporphines and aristolactams, are present herein.

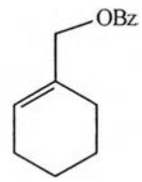
## Cyclohexene derivatives

Cyclohexenes form a small group of plant secondary metabolites which are confined to only a few plant families i.e. Annonaceae, Piperaceae, Zingiberaceae and Euphorbiaceae (genus *Croton*). Approximately 70 naturally occuring cyclohexene derivatives have been found in these plants. Around 10% each of the cyclohexenes were found in Piperaceae and Zingiberaceae, while the rest were exclusively found in the genus *Uvaria* of the Annonaceae. The majority of the polyoxygenated cyclohexenes possess simple molecular skeleton of 1-methylcyclohex-4-ene, although a few derivatives such as piperenols A-C from *Piper cubeb* and *P. clarkii* (Koul *et al.*, 1996; Taneja *et al.*, 1991) and uvacalols A-E from *Uvaria calamistrata* (Zhou, Chen and Yu, 1999) possess the 1-benzoyloxymethylcyclohex-1(6)-ene skeleton instead.

Cyclohexene epoxides and seco-cyclohexenes were also reported (Wang *et al.*, 2003; 2005).




l-methylcyclohex-4-ene




l-benzoyloxymethylcyclohex-1(6)-ene

The biogenetic pathway of cyclohexenes has been proposed (Jolad *et al.*, 1981). The co-occurence of benzyl benzoate, cyclohexenes and *O*-hydroxybenzyl flavanones in the same plant has led to the postulation in which benzyl benzoate acts as the precursor not only of the cyclohexenes, but *O*-hydroxybenzyl dihydrochalcones and flavanones, e.g. chamanetin, isochamanetin and uvaretin, as well (Kodpinid *et al.*, 1985).

A number of cyclohexene derivatives are biologically active. Crotepoxide (Kupchan, Hemingway and Smith, 1969), zeylenone (Liao *et al.*, 1997) and kweichowenol B (Takeuchi *et al.*, 2002) exhibited antitumor activity against a number of cancer cell lines, whereas pipoxide isolated from *Piper pandensis* showed antimalarial activity against the parasite *Plasmodium falciparum* (Nkunya *et al.*, 1987). Distribution of cyclohexene derivatives in the plant kingdom is shown in Table 1, and their structures are shown in **Figure 3**.

**Table 1**. Distribution of cyclohexene derivatives in plants.

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| 2-*O*-Acetyl-6-*O*-benzoylzeylenol **(1.1)** | *Uvaria purpurea* | Annonaceae | Leaves | Takeuchi *et al*., 2002 |
| 2-*O*-Acetyl-6-*O*-methylzeylenol **(1.2)** | *U. purpurea* | Annonaceae | Leaves | Takeuchi *et al*., 2002 |
| 2-*O*-Benzoyl-3-*O*-debenzoylzeylenone **(1.3)** | *U. purpurea* | Annonaceae | Leaves | Takeuchi *et al*., 2002 |
| 1$\alpha$-Benzoyloxymethyl-3$\alpha$-benzoyloxycyclohex-5-en-1$\beta$,2$\beta$,4$\beta$-triol **(1.4)** | *Monanthotaxis buchananii* | Annonaceae | Bark | Liang *et al*., 1988 |
| (+)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-5-acetate **(1.5)** | *Kaempferia rotunda* | Zingiberaceae | Rhizome | Pancharoen, Tuntiwachwutti-kul and Taylor, 1996 |
| (-)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethy-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-6-acetate **(1.6)** | *Kaempferia rotunda* | Zingiberaceae | Rhizome | Pancharoen *et al*., 1996 |
| (-)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-6-benzoate **(1.7)** | *Kaempferia rotunda* | Zingiberaceae | Rhizome | Pancharoen *et al*., 1996 |
| (-)-(1*R*,2*S*,3*R*,4*S*)-2-Benzoyloxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate **(1.8)** | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen, Tuntiwachwutti-kul and Taylor, 1989 |
| Boesenboxide **(1.9)** | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen *et al*., 1989 |
| (+)-Crotepoxide **(1.10)** | *Croton macrostachys* | Euphorbiaceae | n.i. | Kupchan *et al*., 1969a |
| | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen *et al*., 1989 |
| | *Piper cubeb* | Piperaceae | Fruits | Taneja *et al*., 1996 |
| | *Kaempferia rotunda* | Zingiberaceae | Rhizome | Pancharoen *et al*., 1996 |

**Table 1**. Distribution of cyclohexene derivatives in plants (continued).

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| 3-*O*-Debenzoylgrandiflorone (**1.11**) | *Uvaria purpurea* | Annonaceae | Leaves | Takeuchi *et al.*, 2002 |
| 3-*O*-Debenzoylzeylenone (**1.12**) | *U. purpurea* | Annonaceae | Leaves | Takeuchi *et al.*, 2002 |
| (-)-1,6-Desoxysenepoxide (**1.13**) | *U. ferruginea* | Annonaceae | Root | Kodpinid *et al.*, 1985 |
| (-)-1,6-Desoxytingtanoxide (**1.14**) | *U. ferruginea* | Annonaceae | Root | Kodpinid *et al.*, 1985 |
| Ellipeiopsol A (**1.15**) | *Ellipeiopsis cherrevensis* | Annonaceae | Aerial parts | Kijjao *et al.*, 2002 |
| Ellipeiopsol B (**1.16**) | *E. cherrevensis* | Annonaceae | Aerial parts | Kijjao *et al.*, 2002 |
| Ellipeiopsol C (**1.17**) | *E. cherrevensis* | Annonaceae | Aerial parts | Kijjao *et al.*, 2002 |
| Epimonanthadiepoxide (**1.18**) | *Monanthotaxis buchananii* | Annonaceae | Bark | Liang *et al.*, 1988 |
| 1-Epizeylenol (**1.19**) | *Uvaria zeylanica* | Annonaceae | Root | Jolad *et al.*, 1984 |
| | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1995 |
| Ferrudiol (**1.20**) | *U. ferruginea* | Annonaceae | Leaves | Schulte *et al.*, 1982 |
| | *Ellipeiopsis cherrevensis* | Annonaceae | Aerial parts | Kijjao *et al.*, 2002 |
| Grandifloracin (**1.21**) | *Uvaria grandiflora* | Annonaceae | Stem, leaves | Liao *et al.*, 1997 |
| Grandiflorone (**1.22**) | *Uvaria grandiflora* | Annonaceae | Stem, leaves | Liao *et al.*, 1997 |
| | *U. purpurea* | Annonaceae | Leaves | Takeuchi *et al.*, 2002 |
| (1*R*,2*S*,3*R*,4*S*)-2-Hydroxy-methylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate (**1.23**) | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen *et al.*, 1989 |
| Kweichowenol A (**1.24**) | *Uvaria kweichowensis* | Annonaceae | Leaves | Xu *et al.*, 2005 |
| Kweichowenol B (**1.25**) | *U. kweichowensis* | Annonaceae | Leaves | Xu *et al.*, 2005 |

**Table 1**. Distribution of cyclohexene derivatives in plants (continued).

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| 6-Methoxyzeylenol **(1.26)** | *U. purpurea* | Annonaceae | Wood | Takeuchi *et al.*, 2001; 2002 |
| Monanthadiepoxide methyl ether **(1.27)** | *Monanthotaxis buchananii* | Annonaceae | Bark | Liang *et al.*, 1988 |
| (+)-Pandoxide **(1.28)** | *Uvaria pandensis* | Annonaceae | Bark | Nkunya *et al.*, 1987 |
| Piperenol A **(1.29)** | *Piper cubeb, P. clarkii* | Piperaceae | Fruits | Taneja *et al.*, 1991 |
| (+)-Piperenol A triacetate **(1.30)** | *P. cubeb* | Piperaceae | n.i. | Koul *et al.*, 1996 |
| Piperenol B **(1.31)** | *P. cubeb* | Piperaceae | Fruits | Taneja *et al.*, 1991 |
| (-)-Piperenol C **(1.32)** | *Piper cubeb* | Piperaceae | n.i. | Koul *et al.*, 1996 |
| (-)-Pipoxide **(1.33)** | *Uvaria pandensis* | Annonaceae | Bark | Nkunya *et al.*, 1987 |
| | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen *et al.*, 1989 |
| (+)-Pipoxide **(1.34)** | *Uvaria purpurea* | Annonaceae | | Holbert *et al.*, 1979 |
| | *U. pandensis* | Annonaceae | Bark | Nkunya *et al.*, 1987 |
| (+)-Pipoxide-2-methyl ether **(1.35)** | *Monanthotaxis buchananii* | Annonaceae | Bark | Liang *et al.*, 1988 |
| Senediol **(1.36)** | *Piper ribesioides* | Piperaceae | Fruits, stem | Ruangrungsi *et al.*, 1992 |
| Seneol **(1.37)** | *Uvaria catocarpa* | Annonaceae | Fruits | Hollands *et al.*, 1968 |
| $\alpha$-Senepoxide **(1.38)** | *U. catocarpa* | Annonaceae | Fruits | Hollands *et al.*, 1968 |
| | *U. ferruginea* | Annonaceae | Root | Kodpinid *et al.*, 1985 |
| $\beta$-Senepoxide **(1.39)** | *U. ferruginea* | Annonaceae | Root | Kodpinid *et al.*, 1985 |
| Subglain B **(1.40)** | *Uvaria tonkinensis* var. *subglabra* | Annonaceae | | Liu *et al.*, 2003 |
| Tingtanoxide **(1.41)** | *U. ferruginea* | Annonaceae | Root | Kodpinid *et al.*, 1985 |

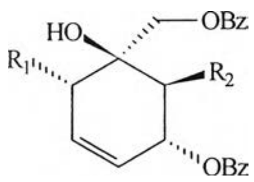
**Table 1**. Distribution of cyclohexene derivatives in plants (continued).

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| Tonkinenin A (**1.42**) | *U. tonkinensis* | Annonaceae | Seeds | Zhao *et al.*, 1996 |
| Uvacalol A (**1.43**) | *U. calamistrata* | Annonaceae | n.i. | Zhou *et al.*, 1999 |
| Uvacalol B (**1.44**) | *U. calamistrata* | Annonaceae | n.i. | Zhou *et al.*, 1999 |
| Uvacalol C (**1.45**) | *U. calamistrata* | Annonaceae | n.i. | Zhou *et al.*, 1999 |
| Uvacalol D (**1.46**) | *U. calamistrata* | Annonaceae | n.i. | Zhou *et al.*, 1999 |
| Uvacalol E (**1.47**) | *U. calamistrata* | Annonaceae | n.i. | Zhou *et al.*, 1999 |
| Uvamalol A (**1.48**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2005 |
| Uvamalol B (**1.49**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2005 |
| Uvamalol C (**1.50**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2005 |
| Uvamalol D (**1.51**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2003 |
| Uvamalol E (**1.52**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2003 |
| Uvamalol F (**1.53**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2003 |
| Uvamalol G (**1.54**) | *U. macrophylla* | Annonaceae | Root | Wang *et al.*, 2003 |
| Uvarigranol A (**1.55**) | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1995 |
| Uvarigranol B (**1.56**) | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1995 |
| Uvarigranol C (**1.57**) | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1995 |
| Uvarigranol D (**1.58**) | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1995 |
| Uvarigranol G (**1.59**) | *U. grandiflora* | Annonaceae | Root | Pan, Chen and Yu, 1998 |
| | *U. kweichowensis* | Annonaceae | Leaves | Xu *et al.*, 2005 |
| Uvarigranol H (**1.60**) | *U. grandiflora* | Annonaceae | Root | Pan *et al.*, 1998 |
| Uvarigranol I (**1.61**) | *U. grandiflora* | Annonaceae | Root | Pan *et al.*, 1998 |
| Zeylena (**1.62**) | *U. zeylanica* | Annonaceae | Root | Jolad *et al.*, 1981 |
| (+)-Zeylenol (**1.63**) | *U. zeylanica* | Annonaceae | Root | Jolad *et al.*, 1981; 1984 |
| | *Kaempferia angustifolia* | Zingiberaceae | Rhizome | Pancharoen *et al.*, 1989 |
| | *Piper cubeb* | Piperaceae | Fruits | Taneja *et al.*, 1991 |
| | *Uvaria grandiflora* | Annonaceae | Root | Pan and Yu, 1995; Liao *et al.*, 1997 |
| | *Ellipeiopsis cherrevensis* | Annonaceae | Aerial parts | Kijjao *et al.*, 2002 |
| | *Uvaria kweichowensis* | Annonaceae | Leaves | Xu *et al.*, 2005 |

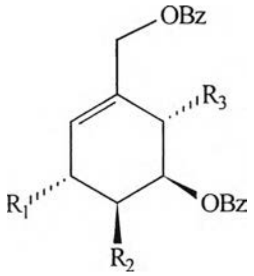
**Table 1**. Distribution of cyclohexene derivatives in plants (continued).

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| (-)-Zeylenol **(1.64)** | *Kaempferia rotunda* | Zingiberaceae | Rhizome | Pancharoen *et al.*, 1996 |
| | *Uvaria purpurea* | Annonaceae | Leaves, wood | Takeuchi *et al.*, 2001; 2002 |
| Zeylenone **(1.65)** | *U. purpurea* | Annonaceae | Wood | Takeuchi *et al.*, 2001 |
| Zeylenyl-2,6-diacetate **(1.66)** | *U. grandiflora* | Annonaceae | Root | Pan and Yu, 1998 |

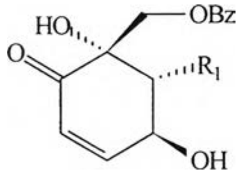
n.i. = not indicated



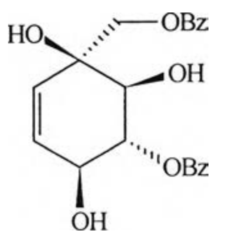

2-*O*-Acetyl-6-*O*-benzoylzeylenol **(1.1)** : $R_1$ = OBz, $R_2$ = OAc
2-*O*-Acetyl-6-*O*-methylzeylenol **(1.2)** : $R_1$ = OMe, $R_2$ = OAc
6-Methoxyzeylenol **(1.26)** : $R_1$ = OMe, $R_2$ = OH
(-)-Zeylenol **(1.64)** : $R_1$ = OMe, $R_2$ = OH




Piperenol A **(1.29)** : $R_1$ = OH, $R_2$ = OH, $R_3$ = OH
(+)-Piperenol A triacetate **(1.30)** : $R_1$ = OAc, $R_2$ = OAc, $R_3$ = OAc

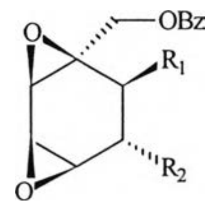



2-*O*-Benzoyl-3-*O*-debenzoylzeylenone **(1.3)** : $R_1$ = OBz
3-*O*-Debenzoylzeylenone **(1.12)** : $R_1$ = OH

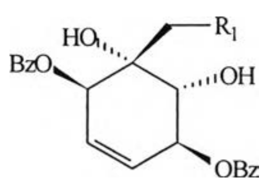



1$\alpha$-Benzoyloxymethyl-3$\alpha$-benzoyloxycyclohex-5-en-1$\beta$,2$\beta$,4$\beta$-triol **(1.4)**

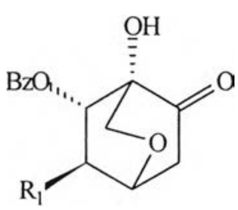
**Figure 3**. Chemical structures of cyclohexene derivatives in plants



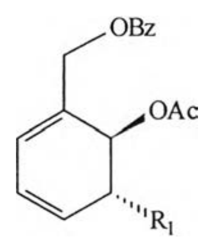
(+)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-5-acetate **(1.5)** : $R_1$ = OAc, $R_2$ = OH
(-)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-6-acetate **(1.6)** : $R_1$ = OH, $R_2$ = OAc
(-)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-Benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0]-octane-5,6-diol-6-benzoate **(1.7)** : $R_1$ = OH, $R_2$ = OBz
Boesenboxide **(1.9)** : $R_1$ = OAc, $R_2$ = OBz
(+)-Crotepoxide **(1.10)** : $R_1$ = OAc, $R_2$ = OAc
Monanthadiepoxide methyl ether **(1.27)** : $R_1$ = $OCH_3$, $R_2$ = OBz



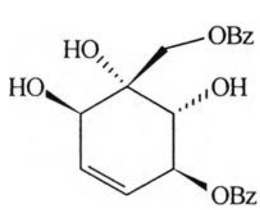
(-)-(1*R*,2*S*,3*R*,4*S*)-2-Benzoyloxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate **(1.8)** : $R_1$ = OBz
(1*R*,2*S*,3*R*,4*S*)-2-Hydroxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate **(1.23)** : $R_1$ = OH



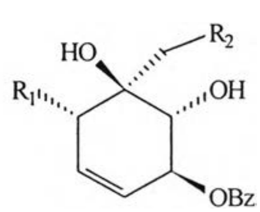
3-*O*-Debenzoylgrandiflorone **(1.11)** : $R_1$ = OH
Grandiflorone **(1.22)** : $R_1$ = OBz



(-)-1,6-Desoxysenepoxide **(1.13)** : $R_1$ = OAc
(-)-1,6-Desoxytingtanoxide **(1.14)** : $R_1$ = OBz

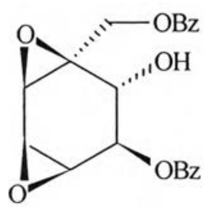


Ellipeiopsol A **(1.15)**

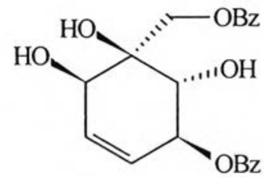


Ellipeiopsol B **(1.16)** : $R_1$ = OH, $R_2$ = OBz
Ellipeiopsol C **(1.17)** : $R_1$ = OBz, $R_2$ = OH
Ferrudiol **(1.20)** : $R_1$ = OBz, $R_2$ = OBz

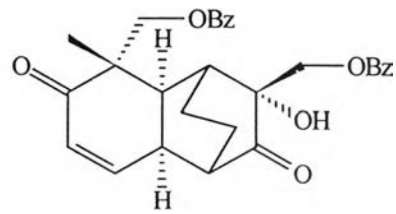
**Figure 3**. Chemical structures of cyclohexene derivatives in plants (continued)



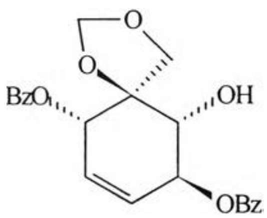
Epimonanthadiepoxide (**1.18**)



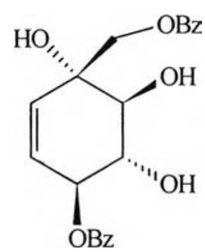
1-Epizeylenol (**1.19**)



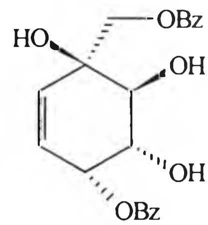
Grandifloracin (**1.21**)



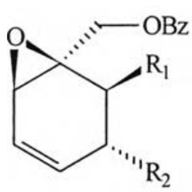
Kweichowenol A (**1.24**)



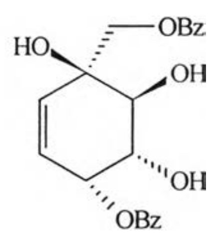
Kweichowenol B (**1.25**)



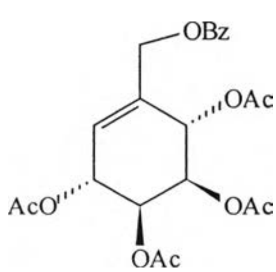
Piperenol B (**1.31**)



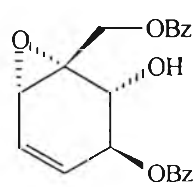
(+)-Pandoxide (**1.28**) : $R_1$ = OAc, $R_2$ = OMe
(+)-Pipoxide (**1.34**) : $R_1$ = OH, $R_2$ = OBz
(+)-Pipoxide-2-methyl ether (**1.35**) : $R_1$ = OMe, $R_2$ = OBz
*β*-Senepoxide (**1.39**) : $R_1$ = OAc, $R_2$ = OAc



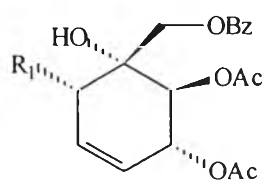
Piperenol B (**1.31**)



(-)-Piperenol C (**1.32**)

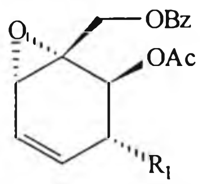


(-)-Pipoxide (**1.33**)

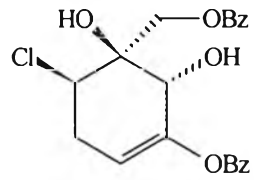


Senediol (**1.36**) : $R_1$ = OH
Seneol (**1.37**) : $R_1$ = OMe

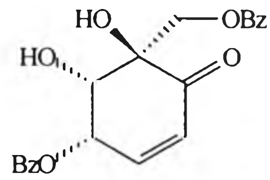
**Figure 3**. Chemical structures of cyclohexene derivatives in plants (continued)



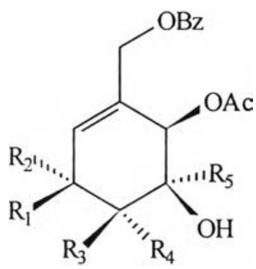
$\alpha$-Senepoxide (**1.38**) : $R_1$ = OAc
Tingtanoxide (**1.41**) : $R_1$ = OBz



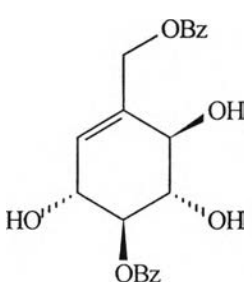
Subglain B (**1.40**)



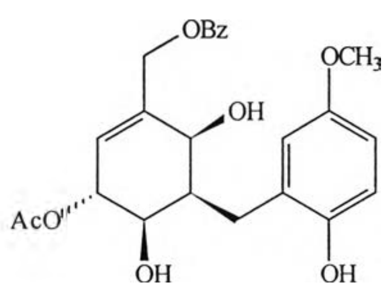
Tonkinenin A (**1.42**)



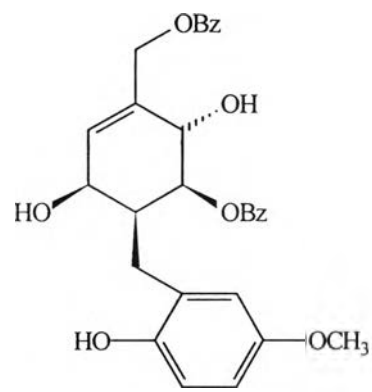
Uvacalol A (**1.43**) : $R_1$ = OEt, $R_2$ = H, $R_3$ = H, $R_4$ = OH, $R_5$ = OBz
Uvacalol B (**1.44**) : $R_1$ = OEt, $R_2$ = H, $R_3$ = OBz, $R_4$ = OH, $R_5$ = H
Uvacalol C (**1.45**) : $R_1$ = OEt, $R_2$ = H, $R_3$ = H, $R_4$ = OH, $R_5$ = OBz
Uvacalol D (**1.46**) : $R_1$ = OH, $R_2$ = H, $R_3$ = H, $R_4$ = H, $R_5$ = OMe
Uvacalol E (**1.47**) : $R_1$ = OBz, $R_2$ = OH, $R_3$ = H, $R_4$ = OH, $R_5$ = H



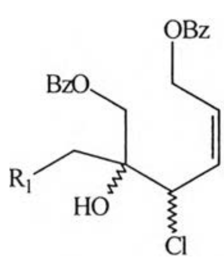
Uvamalol A (**1.48**)



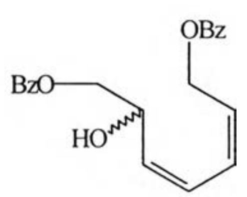
Uvamalol B (**1.49**)



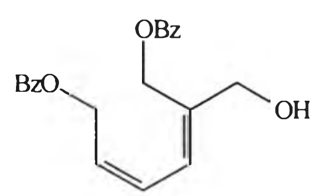
Uvamalol C (**1.50**)



Uvamalol D (**1.51**) : $R_1$ = OAc
Uvamalol E (**1.52**) : $R_1$ = OH

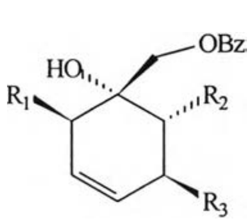


Uvamalol F (**1.53**)

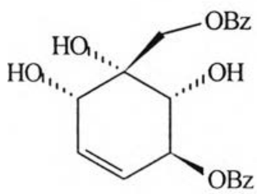


Uvamalol G (**1.54**)

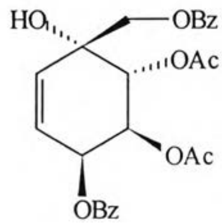
**Figure 3**. Chemical structures of cyclohexene derivatives in plants (continued)



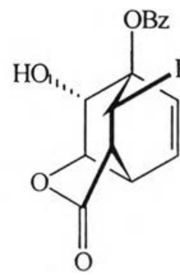

| | |
|---|---|
| Uvarigranol A **(1.55)** | : $R_1$ = OH, $R_2$ = OH, $R_3$ = OH |
| Uvarigranol B **(1.56)** | : $R_1$ = OH, $R_2$ = OAc, $R_3$ = OH |
| Uvarigranol C **(1.57)** | : $R_1$ = OEt, $R_2$ = OH, $R_3$ = OBz |
| Uvarigranol D **(1.58)** | : $R_1$ = OEt, $R_2$ = OAc, $R_3$ = OBz |
| Uvarigranol H **(1.60)** | : $R_1$ = OAc, $R_2$ = OBz, $R_3$ = OBz |



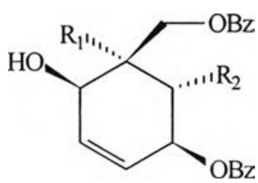

Uvarigranol G **(1.59)**

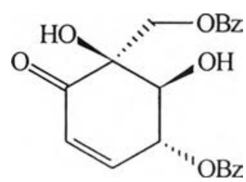



Uvarigranol I **(1.61)**




Zeylena **(1.62)**




(+)-Zeylenol **(1.63)** : $R_1$, $R_2$ = OH
Zeylenyl-2,6-diacetate **(1.66)** : $R_1$, $R_2$ = OAc

Zeylenone **(1.65)**

**Figure 3**. Chemical structures of cyclohexene derivatives in plants (continued)

**Chalconoid compounds**

The term "chalconoid" has been used to define chalcone including dihydrochalcone, chalcane and chalcene. Chalcones appear early in the biosynthetic pathway of flavonoids, acting as precursor for various types of flavonoids. Chalcones can easily be converted to flavanones which can change into flavones, dihydroflavonols, flavonols, flavandiols, catechins or anthocyanidins, according to saturation/unsaturation, oxidation and hydroxylation occuring at the three carbon atoms linking the two aromatic rings (Dewick, 2002).

Chalcones are yellow compounds that are widespread in higher plants and possess a variety of bioactivities including antioxidant, antimalarial, cytotoxic and anti-HIV activities. For example, pedicin, a chalcone from the leaves of *Fissistigma lanuginosum*, was found to inhibit the assembly of tubulin into microtubule, therefore preventing cell division. Two other chalcones from *Desmos dumosus*, fissistin and isofissistin, displayed cytotoxicity to KB cells (Alias *et al.*, 1995), whereas another chalcone, desmosdumotin C was found to be selectively cytotoxic against bone, breast and ovarian cancer cell lines (Wu *et al.*, 2002). Uvaretin from *Uvaria scheffleri*, showed inhibitory activity against malarial protozoa. Anti-HIV activity of chalcones from plants in the genus *Desmos* has also been reported, one of which might be an excellent lead compound for further anti-HIV drug development (Wu *et al.*, 2003)

Interestingly, in the Annonaceae there are special types of chalcones and other flavonoids with the addition of C-benzyl groups. These compounds are quite rare and seem to be limited mostly to the genus *Uvaria*, although a few have also been found in the genera *Desmos* (Rahman, Qais and Rashid, 2003) and *Melodorum* (Jung *et al.*, 1990). Several of these C-benzylated flavonoids were cytotoxic against a number of cancer cell lines. The C-benzylated flavanones: chamanetin, isochamanetin and dichamanetin, and the C-benzylated dihydrochalcones: uvaretin, isouvaretin, and diuvaretin, were responsible for the cytotoxic activity observed in ethanolic extract of the root bark of *Uvaria chamae* (Hufford and Lasswell, 1976; Lasswell and Hufford, 1977a). In addition, uvaretin has been shown to display antibacterial (Hufford and Lasswell, 1976; Nkunya *et al.*, 1993b) and antimalarial activities (Nkunya *et al.*, 1991; Weenen, Nkunya and Mgani, 1991).

Chalconoid compounds from annonaceous plants are summarized in Table 2 and their structure are shown in **Figure 4**.

**Table 2**. Distribution of chalconoid compounds in the Annonaceae

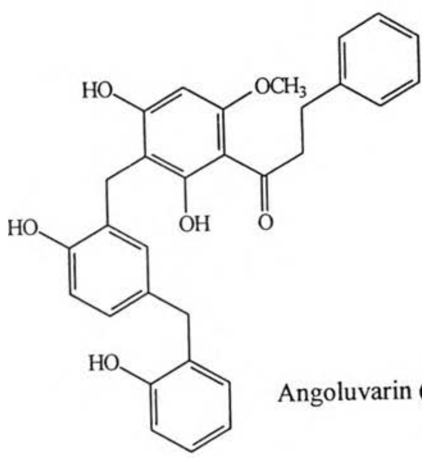
| Compounds | Sources | Part | References |
|---|---|---|---|
| **C-Benzylated dihydrochalcone** Angoluvarin **(2.1)** | *Uvaria angolensis* | Root | Hufford and Oguntimein, 1987 |
| | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| Anguvetin **(2.2)** | *U. angolensis* | Root | Hufford and Oguntimein, 1982 |
| Chamuvaritin **(2.3)** | *U. chamae* | Root | Okorie, 1977 |
| Diuvaretin **(2.4)** | *U. chamae* | Stem bark | Hufford and Lasswell, 1976 |
| | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| Isouvaretin **(2.5)** | *U. angolensis* | Root | Hufford and Oguntimein, 1980 |
| | *U. chamae* | Stem bark | Hufford and Lasswell, 1976 |
| | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| Isotriuvaretin **(2.6)** | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| Triuvaretin **(2.7)** | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| Uvaretin (Chamuvarin) **(2.8)** | *U. acuminata* | Root | Cole, Torrance and Wiedhopf, 1976 |
| | *U. angolensis* | Root | Hufford and Oguntimein, 1980 |
| | *U. chamae* | Root | Hufford and Lasswell, 1976; Okorie, 1977 |
| | *U. kirkii* | Root | Tammami *et al.*, 1977 |
| | *U. leptocladon* | Root bark | Nkunya *et al.*, 1993b |
| | *U. puguensis* | Bark | Makangara, Jonker and Nkunya, 2002 |
| **C-Benzylated chalcone** 2′,4′-Dihydroxy-3′-(2,6-dihydroxybenzyl)-6′-methoxy-chalcone **(2.9)** | *Desmos chinensis* | Leaves | Rahman *et al.*, 2003 |
| **Dihydrochalcone** Angoletin **(2.10)** | *Uvaria angolensis* | Root | Hufford and Oguntimein, 1980 |
| Dihydropedicin **(2.11)** | *Fissistigma lanuginosum* | Leaves | Alias *et al.*, 1995 |
| 2′,3′-Dihydroxy-4′,6′-dimethoxy-dihydrochalcone **(2.12)** | *Anomianthus dulcis* | Leaves | Sinz *et al.*, 1999 |
| | *Uvaria dulcis* | Leaves | Chantrapromma *et al.*, 2000 |
| 2′,4′-Dihydroxy-4,6′-dimethoxy-dihydrochalcone **(2.13)** | *Goniothalamus gardneri* | Aerial parts | Seidel, Bailleul and Waterman, 2000 |

**Table 2.** Distribution of chalconoid compounds in the Annonaceae (continued)

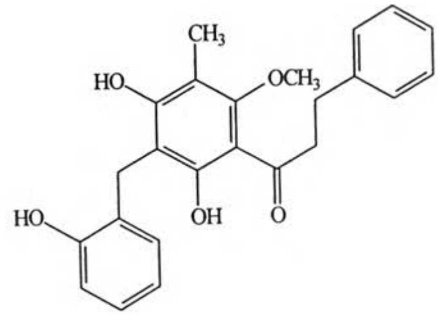
| Compounds | Sources | Part | References |
|---|---|---|---|
| 2′,6′-Dihydroxy-3′,4′-dimethoxy-dihydrochalcone **(2.14)** | *Miliusa balansae* | Leaves branches | Kamperdick, Van and Sung, 2002 |
| 2′,6′-Dihydroxy-4′-methoxy-dihydrochalcone **(2.15)** | *M. kentii* | Bark | Benosman *et al.*, 1997 |
| | *M. balansae* | Leaves, branches | Kamperdick *et al.*, 2002 |
| Flavokawin B **(2.16)** | *Uvaria angolensis* | Root | Hufford and Oguntimein, 1982 |
| 2′-Hydroxy-4,4′,6′-trimethoxy-dihydrochalcone **(2.17)** | *Goniothalamus gardneri* | Aerial parts | Seidel *et al.*, 2000 |
| 2-Hydroxy-3,4,6-trimethoxy-dihydrochalcone **(2.18)** | *Fissistigma bracteolatum* | Leaves | Lien *et al.*, 2000 |
| 2′-Hydroxy-4′,5′,6′-trimethoxy-dihydrochalcone **(2.19)** | *Uvaria mocoli* | Bark | Fleischer, Waigh and Waterman, 1998 |
| (-)-Neolinderatin **(2.20)** | *Mitrella kentii* | Bark | Benosman *et al.*, 1997 |
| (-)-Linderatin **(2.21)** | *M. kentii* | Bark | Benosman *et al.*, 1997 |
| 4,2′,4′-Trihydroxy-6′-methoxy-dihydrochalcone **(2.22)** | *Goniothalamus gardneri* | Aerial parts | Seidel *et al.*, 2000 |
| Uvangoletin **(2.23)** | *Uvaria angolensis* | Root | Hufford and Oguntimein, 1980 |
| **Chalcone** | | | |
| 2′,3′-Dihydroxy-4′,6′-dimethoxy-chalcone **(2.24)** | *Anomianthus dulcis* | Leaves | Sinz *et al.*, 1999 |
| | *Uvaria dulcis* | Leaves | Chantrapromma *et al.*, 2000 |
| 2′,4′-Dihydroxy-4,6′-dimethoxy-chalcone **(2.25)** | *Goniothalamus gardneri* | Aerial parts | Seidel *et al.*, 2000 |
| 2′,6′-Dihydroxy-3′,4′-dimethoxy-chalcone **(2.26)** | *Uvaria scheffleri* | Bark | Nkunya *et al.*, 1990; Moshi *et al.*, 2004 |
| 4′,6′-Dihydroxy-3′,5′-dimethyl-2′-methoxychalcone **(2.27)** | *Cyathocalyx crinatus* | Stem | Shibata *et al.*, 2000 |
| 2′,4-Dihydroxy-3′,4′,6′-trimethoxylchalcone **(2.28)** | *Popowia cauliflora* | Stem | Panichpol and Waterman, 1978 |
| 2′,6′-Dihydroxy-4′-methoxy-chalcone **(2.29)** | *Uvaria scheffleri* | Bark | Nkunya *et al.*, 1990; Moshi *et al.*, 2004 |
| Fissistin **(2.30)** | *Fissistigma lanuginosum* | Leaves | Alias *et al.*, 1995 |
| Flavokawain A **(2.31)** | *Goniothalamus gardneri* | Aerial parts | Seidel *et al.*, 2000 |

**Table 2**. Distribution of chalconoid compounds in the Annonaceae (continued)

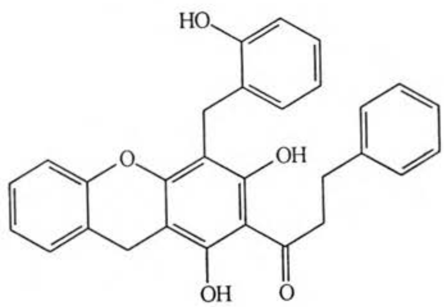
| Compounds | Sources | Part | References |
|---|---|---|---|
| 2′-Hydroxy-4′,6′-dimethoxy-chalcone **(2.32)** | *Uvaria mocoli* | Bark | Fleischer *et al.*, 1998 |
| 2-Hydroxy-3,4,6-trimethoxy-chalcone (Tepanone) **(2.33)** | *Ellipeia cuneifolia* | Root, Bark | Colegate *et al.*, 1992 |
| | *Fissistigma bracteolatum* | Leaves | Lien *et al.*, 2000 |
| | *Uvaria dependens* | Root, Bark | Nkunya *et al.*, 1993a |
| 2′-Hydroxy-4′,5′,6′-trimethoxy-chalcone **(2.34)** | *U. mocoli* | Bark | Fleischer *et al.*, 1998 |
| 2′-Hydroxy-3′,4′,6′-trimethoxy-chalcone **(2.35)** | *Popowia cauliflora* | Stem | Panichpol and Waterman, 1978 |
| | *Uvaria scheffleri* | Bark, Leaves | Nkunya *et al.*, 1990; Moshi *et al.*, 2004 |
| Isofissistin **(2.36)** | *Fissistigma lanuginosum* | Leaves | Alias *et al.*, 1995 |
| Isoschefflerin **(2.37)** | *Uvaria scheffleri* | Bark | Nkunya *et al.*, 1990 |
| 2-Methoxy-3-methyl-4,6-dihydroxy-5-(3′-hydroxy)-cinnamoylbenzaldehyde **(2.38)** | *Desmos sp.* | n.i. | Wu *et al.*, 2003 |
| 3-Methyl-2,4,6-trihydroxy-5-(3′-hydroxy)cinnamoylbenzaldehyde **(2.39)** | *Desmos sp.* | n.i. | Wu *et al.*, 2003 |
| Pedicin **(2.40)** | *Fissistigma lanuginosum* | Leaves | Alias *et al.*, 1995 |
| Schefflerin **(2.41)** | *Uvaria scheffleri* | Bark | Nkunya *et al.*, 1990 |
| 2′,3′,4′,6′-Tetramethoxychalcone **(2.42)** | *Popowia cauliflora* | Stem | Panichpol and Waterman, 1978 |
| **Chalcane** 2′-Hydroxy-3′,4′,6′-trimethoxy-$\beta'$-ethoxychalcane **(2.43)** | *Fissistigma bracteolatum* | Leaves | Lien *et al.*, 2000 |
| 2′-Hydroxy-3′,4′,6′-trimethoxy-$\beta'$-methoxychalcane **(2.44)** | *F. bracteolatum* | Leaves | Lien *et al.*, 2000 |
| **Chalcene** 2-Hydroxy-3,4,6-trimethoxy-chalcene **(2.45)** | *F. bracteolatum* | Leaves | Lien *et al.*, 2000 |



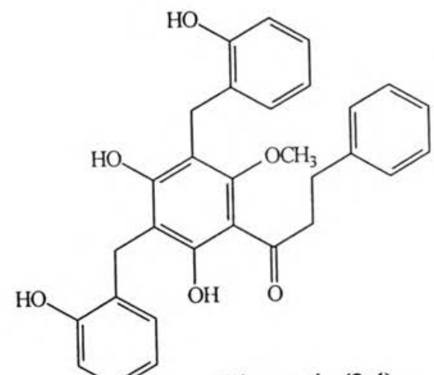
Angoluvarin **(2.1)**



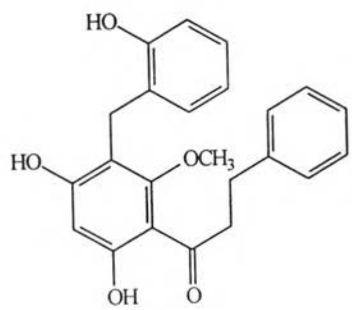
Anguvetin **(2.2)**



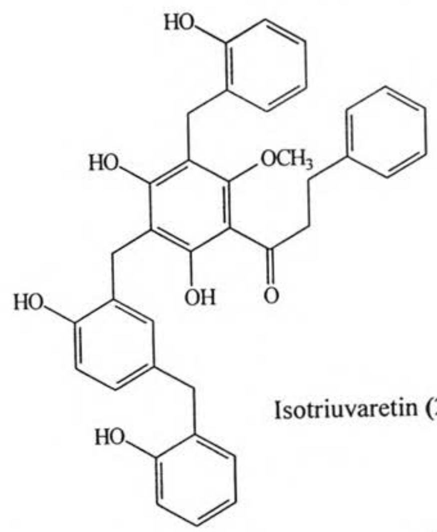
Chamuvaritin **(2.3)**



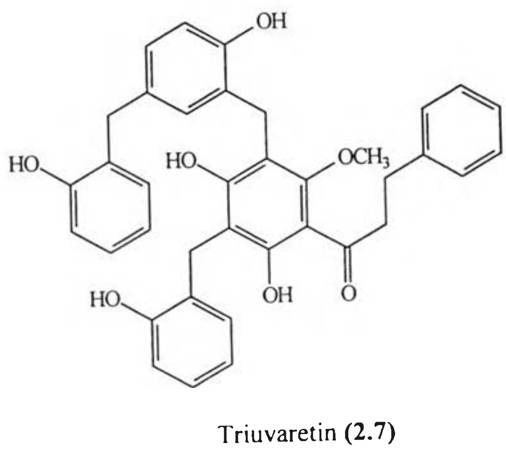
Diuvaretin **(2.4)**



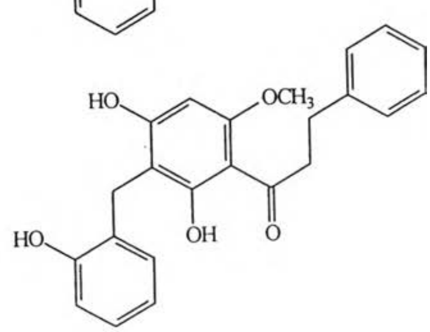
Isouvaretin **(2.5)**



Isotriuvaretin **(2.6)**

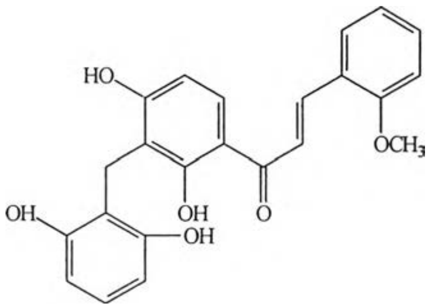


Triuvaretin **(2.7)**

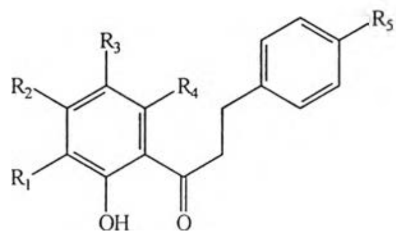


Uvaretin **(2.8)**

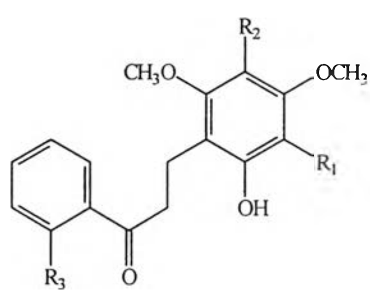
**Figure 4**. Chemical structures of chalconoid compounds in the Annonaceae



2′,4′-Dihydroxy-3′-(2,6-dihydroxybenzyl)-6′-methoxychalcone (**2.9**)

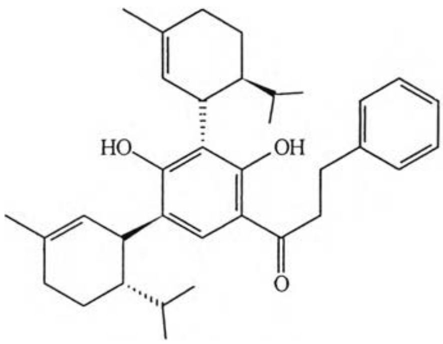


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ |
|---|---|---|---|---|---|
| Angoletin (**2.10**) | $CH_3$ | OH | $CH_3$ | $OCH_3$ | H |
| Dihydropedicin (**2.11**) | $OCH_3$ | $OCH_3$ | $CH_3$ | $OCH_3$ | H |
| 2′,3′-Dihydroxy-4′,6′-dimethoxy-dihydrochalcone (**2.12**) | OH | $OCH_3$ | H | $OCH_3$ | H |
| 2′,4′-Dihydroxy-4,6′-dimethoxy-dihydrochalcone (**2.13**) | H | OH | H | $OCH_3$ | $OCH_3$ |
| 2′,6′-Dihydroxy-3′,4′-dimethoxy-dihydrochalcone (**2.14**) | $OCH_3$ | $OCH_3$ | H | OH | H |
| 2′,6′-Dihydroxy-4′-methoxy-dihydrochalcone (**2.15**) | H | $OCH_3$ | H | OH | H |
| Flavokawin B (**2.16**) | H | $OCH_3$ | H | $OCH_3$ | H |
| 2′-Hydroxy-4,4′,6′-trimethoxy-dihydrochalcone (**2.17**) | H | $OCH_3$ | H | $OCH_3$ | $OCH_3$ |
| 2′-Hydroxy-4′,5′,6′-trimethoxy-dihydrochalcone (**2.19**) | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| 4,2′,4′-Trihydroxy-6′-methoxy-dihydrochalcone (**2.22**) | H | OH | H | $OCH_3$ | OH |
| Uvangoletin (**2.23**) | H | OH | H | $OCH_3$ | H |

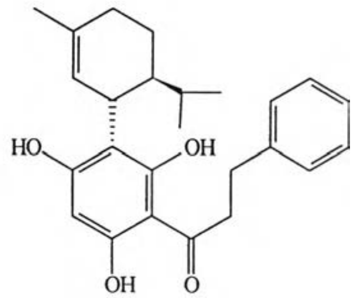


| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 2-Hydroxy-3,4,6-trimethox, -dihydrochalcone (**2.17**) | $OCH_3$ | H | OH |
| 2-Hydroxy-4,5,6-trimethoxy-dihydrochalcone (**2.18**) | H | $OCH_3$ | H |

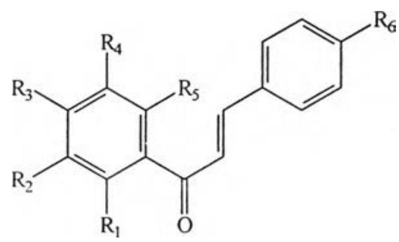
**Figure 4**. Chemical structures of chalconoid compounds in the Annonaceae (continued)



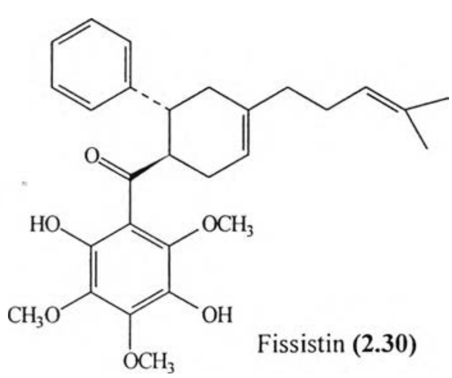
(-)-Neolinderatin **(2.20)**



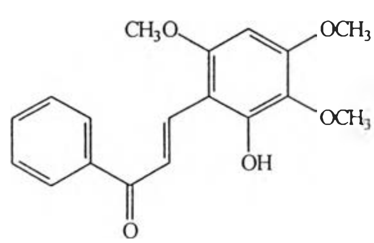
(-)-Linderatin **(2.21)**



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| 2′,3′-Dihydroxy-4′,6′-dimethoxy-chalcone **(2.24)** | OH | OH | $OCH_3$ | H | $OCH_3$ | H |
| 2′,4′-Dihydroxy-4,6′-dimethoxy-chalcone **(2.25)** | OH | H | OH | H | $OCH_3$ | $OCH_3$ |
| 2′,6′-Dihydroxy-3′,4′-dimethoxy-chalcone **(2.26)** | OH | $OCH_3$ | $OCH_3$ | H | OH | H |
| 4′,6′-Dihydroxy-3′,5′-dimethyl-2′-methoxychalcone **(2.27)** | $OCH_3$ | $CH_3$ | OH | $CH_3$ | OH | H |
| 2′,4-Dihydroxy-3′,4′,6′-trimethoxy-chalcone **(2.28)** | OH | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | OH |
| 2′,6′-Dihydroxy-4′-methoxy-chalcone **(2.29)** | OH | H | $OCH_3$ | H | OH | H |
| Flavokawain A **(2.31)** | OH | H | $OCH_3$ | H | $OCH_3$ | $OCH_3$ |
| 2′-Hydroxy-4′,6′-dimethoxy-chalcone **(2.32)** | OH | H | $OCH_3$ | H | $OCH_3$ | H |
| 2′-Hydroxy-4′,5′,6′-trimethoxy-chalcone **(2.34)** | OH | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| 2′-Hydroxy-3′,4′,6″-trimethoxy-chalcone **(2.35)** | OH | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | H |
| Pedicine **(2.40)** | OH | $OCH_3$ | $OCH_3$ | OH | $OCH_3$ | H |
| 2′,3′,4′,6′-Tetramethoxychalcone **(2.42)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | H |

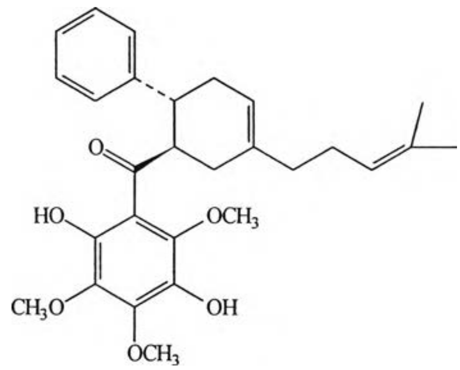


Fissistin **(2.30)**

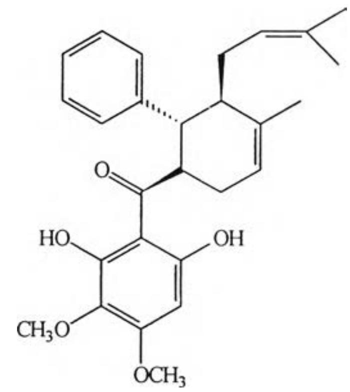


2-Hydroxy-3,4,6-trimethoxychalcone **(2.33)**

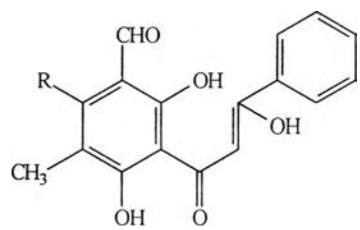
**Figure 4**. Chemical structures of chalconoid compounds in the Annonaceae (continued)



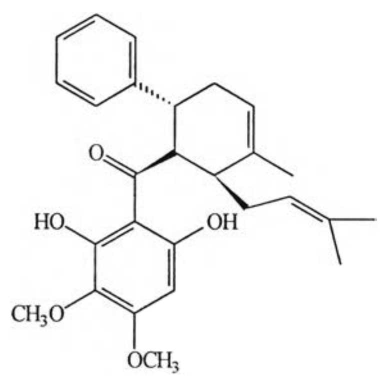
Isofissistin (**2.36**)



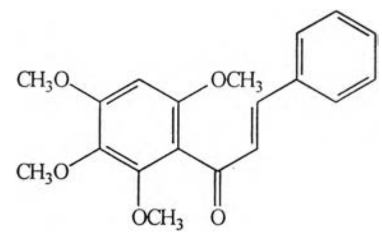
Isoschefflerin (**2.37**)



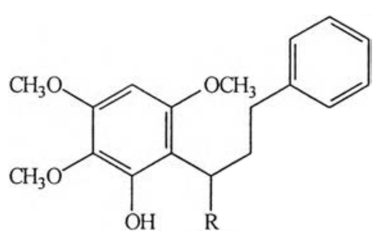
2-Methoxy-3-methyl-4,6-dihydroxy-5-(3′-hydroxy)cinnamoylbenzaldehyde (**2.38**) : R = $OCH_3$
3-Methyl-2,4,6-trihydroxy-5-(3′-hydroxy)cinnamoylbenzaldehyde (**2.39**) : R = OH



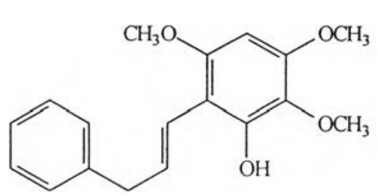
Schefflerin (**2.41**)



2′,3′,4′,6′-Tetramethoxychalcone (**2.42**)



2′-Hydroxy-3′,4′,6′-trimethoxy-*β*′-ethoxychalcane (**2.43**) : R = $OC_2H_5$
2′-Hydroxy-3′,4′,6′-trimethoxy-*β*′-methoxychalcane (**2.44**) : R = $OCH_3$



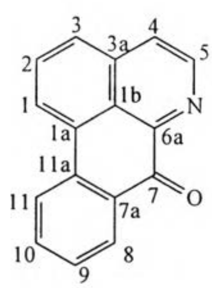
2-Hydroxy-3,4,6-trimethoxychalcene (**2.45**)

**Figure 4**. Chemical structures of chalconoid compounds in the Annonaceae (continued)

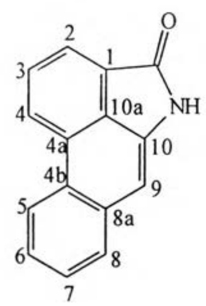
**Oxoaporphine, dioxoaporphine and aristolactam alkaloids**

The aporphine alkaloids are one of the largest subgroups of isoquinoline alkaloids found in the superorder Magnoliidae (which includes the orders Magnoliales, Illiciales, Laurales, Piperales, Aristolochiales and Ranunculales).

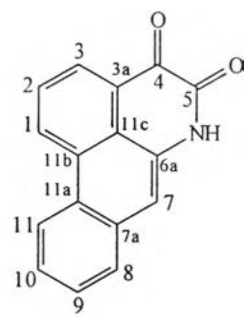
Aporphinoid alkaloids can be classified into nine groups (Bentley, 2003) which are 1) Proaporphines, 2) Aporphinoids, 3) Dimeric aporphines, 4) Aporphine-benzylisoquinoline dimers, 5) Secoaporphines, 6) Oxoaporphines, 7) Dioxoaporphines, 8) Aristolactams and 9) Oxoisoaporphines. In this review, oxoaporphines, dioxoaporphines and aristolactams will be discussed.



Oxoaporphine



Aristolactam



4,5-Dioxoaporphine

Although the family Annonaceae is the main source of oxoaporphines, they can also be found in other families such as Menispermaceae e.g. oxostephanine from *Stephania japonica* (Watanabe *et al.*, 1975), oxoxylopine from *Stephania abssinica* (Kupchan, Suffness and Gordon, 1969b), as well as liriodenine and dicentrinone from *Stephania dinklagei* (Camacho *et al.*, 2000).

The dioxoaporphines are a small group of aporphine alkaloids found mostly in the families Menispermaceae e.g. stephadione from the aerial part of *Stephania tetrandra* (Si, Zhao and Deng, 1992), Berberidaceae, Annonaceae, Fumariaceae and Aristolochiaceae. However, they can also be found in two other closely related families; Piperaceae and Saururaceae. Examples are norcepharadione B, from *Houttuynia cordata* (family Saururaceae) (Probstle and Bauer, 1992) and several dioxoaporphines found in several plants in the family Piperaceae e.g. *Piper longum* (Desai, Prabhu and Mulchandani, 1988) and *Piper canium* (Ma *et al.*, 2004b).

Aristolactams are a small group of compounds found mainly in the family Aristolochiaceae. They are also report as constituents in the families Annonaceae, Monimiaceae, Menispermaceae and Piperaceae (e.g. Caldensin from *Piper caldense* (Cardozo and Chaves, 2003). They are also known as phenanthrene lactams because their structures contain both phenanthrene chromophore and lactam groups. Although the aristolactams are non-basic, they are classified as aporphine alkaloids since their skeleton bears a distinct similarity to that of the aporphines (Kumar *et al.*, 2003).

One of the most important physical characteristics of aristolactams, oxo- and dioxoaporphines is their ability to fluoresce under UV light due to their highly conjugated structure. The co-isolation of aristolactam and 4,5-dioxoaporphines from plants of the Aristolochiaceae (Probstle and Bauer, 1992), Menispermaceae, Annonaceae (Chia *et al.*, 2000) and Piperaceae (Desai *et al.*, 1988; Chen *et al.*, 2004) has led to the hypothesis that 4,5-dioxoaporphines might arise from oxidation of the aporphines and function as intermediates in the biosynthesis of aristolactams (Castedo, Suau and Mourino, 1976). In fact, conversion of a 4,5-dioxoaporphine into an aristolactam took place *in vitro* and was regarded as benzylic acid rearrangement, followed by loss of a carbon atom.

These alkaloids displayed biological activities which are antiprotozoal e.g. antimycobacterial aristolactams from *Piper sanctum* (Mata *et al.*, 2004), antifungal and cytotoxic activities. A widely found oxoaporphine alkaloid, liriodenine, was reported as being potently cytotoxic against KB, human lung carcinoma (A-549), human colon tumour (HCT-8), P-388 and L-1210 cell lines with $ED_{50}$ values of 1.00, 0.72, 0,70, 0.57 and 2.33 μg/ml, respectively (Wu *et al.*, 1989). It was shown to be an inhibitor of the enzyme topoisomerase II by DNA-intercalating mechanism (Woo *et al.*, 1997; 1999). In addition, liriodenine has also been found to have potent antifungal (Nissanka *et al.*, 2001) and antiprotozoal activities against *Leishmania donovani* and *Plasmodium falciparum* (Camacho *et al.*, 2000). Other oxoaporphine alkaloids are oxostephanine, which exhibited selective toxicity to HeLa (uterus carcinoma) cell line and also decreased mitotic index in both HeLa and SKVO3 (ovary carcinoma) cell lines (Rodriguez *et al.*, 1999); artherospermidine, which was potently effective against hepatocarcinoma cell lines Hep $G_2$ and Hep 2,2,15 with $IC_{50}$ values of 0.8 and 2.2 μg/ml, respectively (Hsieh *et al.*, 2001); *O*-methylmoschatoline from the bark of *Cananga odorata* which showed antibacterial activity against gram positive and negative bacteria, antifungal activity and cytotoxicity in brine shrimp bioassay (Rahman *et al.*, 2005); oxoglaucine, which exerted immunomodulatory effect *in vivo* (Ivanovska, Philiper and Georgieva, 1997) and also exhibited antiplatelet aggregration activity (Chang *et al.*, 1998). Both the dioxoaporphine artabotrine and the oxoaporphine artherospermidine, from *Artabotrys zeylanicus* were cytotoxic to P-388 cell line (Wijeratne *et al.*, 1995).

Three aristolactam alkaloids: aristolactams A, B and piperolactam A, together with the 4,5-dioxoaporphines: norcepharadione B, cepharadione B and splendidine, from aerial part of *Houttuynia cordata* exhibited cytotoxicity against A-549, SK-OV-3, SK-MEL-2, XF0498 and HCT-15 cancer cell lines (Kim *et al.*, 2001). Piperolactams B, C, aristolactam B III and goniothalactam all possessed anti-platelet aggregration activity, as well as aristolactams from *Piper taiwanense* (Chen *et al.*, 2004), while aristolactam B III and goniothalactam were also cytotoxic against P-388, HT-29 and A549 cell lines (Tsai *et al.*, 2005).

Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae is summarized in Table 3. Their chemical structures are shown in **Figure 5**.

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae

| Compounds | Sources | Part | References |
|---|---|---|---|
| **Oxoaporphine alkaloids** | | | |
| Annolatine **(3.1)** | *Annona montana* | Leaves | Wu *et al.*, 1993 |
| Artabonatine C **(3.2)** | *Artabotrys uncinatus* | Root | Hsieh *et al.*, 2001 |
| | *Guatteria amplifolia* | Leaves | Montenegro *et al.*, 2003 |
| | *G. multivenia* | Root | Zhang *et al.*, 2002 |
| Artabonatine D **(3.3)** | *Artabotrys uncinatus* | Root | Hsieh *et al.*, 2001 |
| Artherospermidine **(3.4)** | *A. uncinatus* | Stem | Wu *et al.*, 1989 |
| | *A. zeylanicus* | Stem bark | Wijeratne *et al.*, 1995 |
| | *Fissistigma glaucescens* | Leaves | Lo, Chang and Wu, 2000 |
| | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| | *Pseuduvaria indochinensis* | Bark | Zhong, Zhao and Xie, 1988 |
| Dicentrinone **(3.5)** | *Desmos dasymaschalus* | Leaves | Chan and Toh, 1986 |
| 1,9-Dihydroxy-2,11-dimethoxy-4,5-dihydro-7-oxoaporphine **(3.6)** | *Miliusa cuneata* | Stem, leaves | Chen *et al.*, 2003 |
| 1,2-Dimethoxy-3-hydroxy-5-oxonoraporphine **(3.7)** | *Mitrephora cf. maingayi* | Bark | Lee, Xu and Goh, 1999 |
| Fissicesine **(3.8)** | *Fissistigma glaucescens* | Leaves | Lo *et al.*, 2000 |
| 10-Hydroxyliriodenine **(3.9)** | *Miliusa cf. banacea* | Root | Harrigan *et al.*, 1994 |
| | *M. velutina* | Bark | Jumana, Hasan and Rashid, 2000 |
| 11-Hydroxy-1,2-methylene-dioxyoxoaporphine **(3.10)** | *Duguetia eximia* | Wood | Gottlieb *et al.*, 1978 |
| Kaufumine **(3.11)** | *Fissistigma glaucescens* | Leaves | Lo *et al.*, 2000 |
| Lanuginosine **(3.12)** | *Annona squamosa* | Leaves | Bhaumik *et al.*, 1979 |
| | *Guatteria multivenia* | Root | Zhang *et al.*, 2002 |
| | *Miliusa cuneata* | Stem, leaves | Chen *et al.*, 2003 |
| | *Xylopia lemurica* | Wood | Nieto, Leboeuf and Cave, 1975 |

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

| Compounds | Sources | Part | References |
|---|---|---|---|
| Liriodenine **(3.13)** | *Annona glabra* | Fruits | Chang *et al.*, 2000 |
| | *A. montana* | Leaves | Wu *et al.*, 1993 |
| | *A. squamosa* | Root | Perez-Amador *et al.*, 2004 |
| | *Artabotrys uncinatus* | Stem | Wu *et al*, 1989 |
| | *Cananga odorata* | Bark | Rahman *et al.*, 2005 |
| | *Fissistigma glaucescens* | Wood | Lu, Wu and Leou, 1985; Lo *et al.*, 2000 |
| | *Fusea longifolia* | Wood | Braz *et al.*, 1976 |
| | *Goniothalamus amuyon* | Wood | Lu *et al.*, 1985 |
| | *Guatteria diospyroides* | Root | Perez-Amador *et al.*, 2004 |
| | *G. goudotiana* | Leaves | Castedo *et al.*, 1991 |
| | *G. multivenia* | Root | Zhang *et al.*, 2002 |
| | *G. oliviformis* | Stem | Lopez *et al.*, 1990 |
| | *Lettowianthus stellatus* | Root, Bark | Nkunya *et al.*, 2000 |
| | *Miliusa cuneata* | Stem, leaves | Chen *et al.*, 2003 |
| | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| | *Pseuduvaria indochinensis* | Bark | Zhong *et al.*, 1988 |
| | *Uvariopsis guineensis* | Bark | Leboeuf and Cave, 1972 |
| | *Uvaria macoli* | Bark | Fleischer *et al.*, 1998 |
| | *Xylopia aethiopica* | Root | Harrigan *et al.*, 1994 |
| Lysicamine **(3.14)** | *Annona glabra* | Fruits | Chang *et al.*, 2000 |
| | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| | *Xylopia aethiopica* | Root | Harrigan *et al.*, 1994 |
| 10-Methoxyliriodenine **(3.15)** | *Miliusa cf. banacea* | Root | Harrigan *et al.*, 1994 |
| | *M. velutina* | Bark | Jumana *et al.*, 2000 |
| 11-Methoxy-1,2-methylene-dioxyoxoaporphine **(3.16)** | *Duguetia eximia* | Wood | Gottlieb *et al.*, 1978 |
| 3-Methoxysampangine **(3.17)** | *D. hadrantha* | Bark | Muhammad *et al.*, 2001 |

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

| Compounds | Sources | Part | References |
|---|---|---|---|
| *O*-Methylmoschatoline **(3.18)** | *Cananga odorata* | Bark | Rahman *et al.*, 2005 |
| | *Duguetia eximia* | Wood | Gottlieb *et al.*, 1978 |
| | *Guatteria tonduzii* | Leaves | Lopez *et al.*, 1990 |
| | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| | *Pseuduvaria macrophylla* | Bark | Mahmood *et al.*, 1986a |
| | *Xylopia aethiopica* | Twigs, leaves, stem bark | Harrigan *et al.*, 1994 |
| Oxoanalobine **(3.19)** | *Annona squamosa* | Root | Perez-Amador *et al.*, 2004 |
| | *Guatteria diospyroides* | Root | Perez-Amador *et al.*, 2004 |
| | *Pseuduvaria indochinensis* | Bark | Zhong *et al.*, 1988 |
| Oxoaporphine-3-methoxy-oxoputerine **(3.20)** | *Guatteria foliosa* | Bark | Mahiou *et al.*, 1994 |
| Oxobuxifolina **(3.21)** | *Duguetia glabriuscula* | Bark | Siqueira *et al.*, 2001 |
| | *Uvaria macoli* | Bark | Fleischer *et al.*, 1998 |
| | *Xylopia aethiopica* | Root | Harrigan *et al.*, 1994 |
| Oxocrebanine **(3.22)** | *Fissistigma glaucescens* | Wood, leaves | Lu *et al.*, 1985; Lo *et al.*, 2000 |
| Oxoglaucine **(3.23)** | *Annona purpurea* | Leaves | Chang *et al.*, 1998 |
| | *Glaucium flavum* | Aerial parts | Ivanovska *et al.*, 1997 |
| Oxophoebine **(3.24)** | *Xylopia aethiopica* | Root | Harrigan *et al.*, 1994 |
| Oxostephanine **(3.25)** | *Duguetia eximea* | Wood | Gottlieb *et al.*, 1978 |
| | *Goniothalamus malayanus* | Leaves, bark | Ee, Lee and Goh, 1999 |
| | *Guatteria calva* | Leaves | Rodriguez *et al.*, 1999 |
| | *Goniothalamus uvariodes* | Leaves, bark | Ee *et al.*, 1999 |
| | *G. velutinus* | Leaves, bark | Ee *et al.*, 1999 |
| | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| | *P. insignis* | Bark | Lee, Chuah and Goh, 1997 |
| Oxoxylopine **(3.26)** | *Fissistigma glaucescens* | Leaves | Lo *et al.*, 2000 |
| Sampangine **(3.27)** | *Duguetia hadrantha* | Bark | Muhammad *et al.*, 2001 |
| Thailandine **(3.28)** | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

| Compounds | Sources | Part | References |
|---|---|---|---|
| 1,2,3-Trimethoxy-5-oxonor-aporphine **(3.29)** | *Mitrephora cf. maingayi* | Bark | Lee *et al.*,1999 |
| **Dioxoaporphine alkaloids** Artabotrine **(3.30)** | *Artabotrys zeylanicus* | Bark | Wijeratne *et al.*, 1995 |
| 4,5-Dioxodehydroasimilobin **(3.31)** | *Uvaria macrocarpa* | n.i. | Kumar *et al.*, 2003 |
| Griffithidione **(3.32)** | *Goniothalamus griffthii* | n.i. | Kumar *et al.*, 2003 |
| Hadranthine A **(3.33)** | *Duguetia hadrantha* | Bark | Muhammad *et al.*, 2001 |
| Hadranthine B **(3.34)** | *D. hadrantha* | Bark | Muhammad *et al.*, 2001 |
| Imbiline-1 **(3.35)** | *D. hadrantha* | Bark | Muhammad *et al.*, 2001 |
| Labeccapolydione **(3.36)** | *Polyalthia cauliflora* | n.i. | Jossang *et al.*, 1984 |
| Lettowianthine **(3.37)** | *Lettowianthus stellatus* | Root bark | Nkunya *et al.*, 2000 |
| 3-Methoxycepharadione B **(3.38)** | *Mitrephora maingayi* | Stem bark | Lee *et al.*, 1999 |
| 11-Methoxylettowianthine **(3.39)** | *Lettowianthus stellatus* | Root bark | Nkunya *et al.*, 2000 |
| 8-Methoxyouregidione **(3.40)** | *Artabotrys zeylanicus* | Bark | Wijeratne *et al.*, 1995 |
| N-Methylouregidione **(3.41)** | *Pseuduvaria macrophylla* | Bark | Mahmood *et al.*, 1986a |
| Noraristolodione **(3.42)** | *Fissistigma balanse* | Twigs | Chia *et al.*, 2000 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| Norcepharadione A **(3.43)** | *Annona hayesii* | n.i. | Rasamizafy *et al.*, 1987 |
| Norcepharadione B **(3.44)** | *Fissistigma balanse* | Twigs | Chia *et al.*, 2000 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| | *Guatteria ouregou* | Bark, leaves | Cortes *et al.*, 1986 |
| | *Goniothalamus tenuifolius* | Bark | Likhitwittayawuid *et al.*, 1997 |
| | *Oxymitra velutina* | Leaves, twigs | Achenbach and Hemrich, 1991 |
| Ouregidione **(3.45)** | *Artabotrys zeylanicus* | Bark | Wijeratne *et al.*, 1996 |
| | *Goniothalamus malayanus* | n.i. | Kumar *et al.*, 2003 |
| | *G. velutinus* | n.i. | Kumar *et al.*, 2003 |
| | *Gautteria ouregou* | Bark, leaves | Cortes *et al.*, 1986 |

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

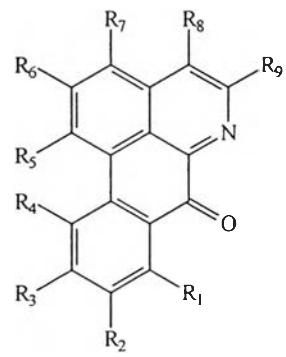
| Compounds | Sources | Part | References |
|---|---|---|---|
| **Aristolactam alkaloids** | | | |
| 10-Amino-4,8-dihydroxy-3-methoxyphenanthere-1-carboxylic acid lactam **(3.46)** | *Goniothalamus cheliensis* | n.i. | Kumar *et al.*, 2003 |
| 10-Amino-2,3-dimethoxy-phenanthrene-1-carboxylic acid lactam **(3.47)** | *G. griffithii* | n.i. | Kumar *et al.*, 2003 |
| Aristolactam II (Cepharanone A) **(3.48)** | *Schefferomitra subaequalis* | Bark | Dyke and Gellert, 1978 |
| Aristolactam A Ia **(3.49)** | *Uvaria grandiflora* | n.i. | Kumar *et al.*, 2003 |
| | *U. microcarpa* | n.i. | Kumar *et al.*, 2003 |
| Aristolactam A II **(3.50)** | *Annona cacans* | Stem | Saito and Alvarenga, 1994 |
| | *Aristolochia argentina* | Rhizome | Crohare *et al.*, 1974; Priestap, 1985 |
| | *A. indica* | Root | Achari *et al.*, 1982 |
| | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *F. bracteolatum* | Stem | Lan *et al.*, 2005 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| | *F. oldhamii* | Stem | Chia *et al.*, 2000 |
| | *Goniothalamus cheliensis* | n.i. | Kumar *et al.*, 2003 |
| | *G. griffithii* | Root | Zhang *et al.*, 1999 |
| | *G. sesquipedalis* | Leaves, twigs | Talapatra *et al.*, 1988 |
| | *G. tenuifolius* | Bark | Likhitwitayawuid *et al.*, 1997 |
| | *Uvaria microcarpa* | n.i. | Kumar *et al.*, 2003 |
| Aristolactam A III **(3.51)** | *Goniothalamus borneensis* | Bark | Cao *et al.*, 1998 |
| | *Uvaria hamiltonii* | Bark | Hasan, Asha and Rashid, 2001 |
| Aristolactam A IIIa **(3.52)** | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *Goniothalamus cheliensis* | n.i. | Kumar *et al.*, 2003 |

**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

| Compounds | Sources | Part | References |
|---|---|---|---|
| Aristolactam B I (Taliscanine) **(3.53)** | *Goniothalamus griffithi* | Root | Zhang *et al.*, 1999 |
| | *G. sesquipedalis* | Leaves, twigs | Talapatra *et al.*, 1988 |
| | *G. tenuifolius* | Bark | Likhitwitayawuid *et al.*, 1997 |
| | *Oxymitra velutina* | Twigs | Achenbach and Hemrich, 1991 |
| | *Stelechocarpus burahol* | Bark | Sunardi *et al.*, 2003 |
| | *Uvaria microcarpa* | n.i. | Kumar *et al.*, 2003 |
| Aristolactam B II (Cepharanone B) **(3.54)** | *Annona cacans* | Stem | Saito and Alvarenga, 1994 |
| | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *F. bracteolatum* | Stem | Lan *et al.*, 2005 |
| | *F. glaucescens* | n.i. | Kumar *et al.*, 2003 |
| | *Goniothalamus andersonii* | n.i. | Kumar *et al.*, 2003 |
| | *G. griffithii* | Root | Zhang *et al.*, 1999 |
| | *G. malayanus* | n.i. | Kumar *et al.*, 2003 |
| | *G. tenuifolius* | Bark | Likhitwitayawuid *et al.*, 1997 |
| | *G. velutinus* | Bark | Omar *et al.*, 1992, 79 |
| | *Schefferomitra subequalis* | Bark | Dyke and Gellert, 1978 |
| | *Stelechocarpus burahol* | Bark | Sunardi *et al.*, 2003 |
| | *Uvaria hamiltonii* | Bark | Hasan *et al.*, 2001 |
| | *U. microcarpa* | n.i. | Kumar *et al.*, 2003 |
| Aristolactam B III **(3.55)** | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *F. bracteolatum* | Stem | Lan *et al.*, 2005 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| | *F. oldhamii* | Stem | Chia *et al.*, 2000 |
| Aristolactam F II (Goniopedaline) **(3.56)** | *F. oldhamii* | Stem | Chia *et al.*, 2000 |
| | *Goniothalamus sesquipedalis* | Leaves, twigs | Talapatra *et al.*, 1988 |
| | *Uvaria hamiltonii* | Bark | Hasan *et al.*, 2001 |
| Aristolamide-*N*-hexoside **(3.57)** | *U. grandiflora* | n.i. | Kumar *et al.*, 2003 |
| *N*,*O*-Diacetylaristolactam AII **(3.58)** | *Goniothalamus sesquipedalis* | Leaves, twig | Talapatra *et al.*, 1988 |

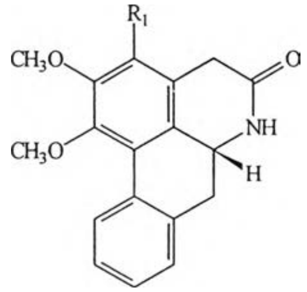
**Table 3.** Distribution of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

| Compounds | Sources | Part | References |
|---|---|---|---|
| Enterocarpam I **(3.59)** | *Fisstigma oldhamii* | Stem | Chia *et al.*, 2000 |
| | *Orophea enterocarpa* | Bark | Mahmood *et al.*, 1986b |
| Enterocarpam II **(3.60)** | *O. enterocarpa* | Bark | Mahmood *et al.*, 1986b |
| Goniothalactam **(3.61)** | *Fisstigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| | *Goniothalamus borneensis* | Bark | Cao *et al.*, 1998 |
| Griffithinam (Gonioffithine, Uvarilactam) **(3.62)** | *G. cheliensis* | n.i. | Kumar *et al.*, 2003 |
| | *G. griffithii* | Root | Zhang *et al.*, 1999 |
| | *Uvaria hamiltonii* | Bark | Hasan *et al.*, 2001 |
| | *U. microcarpa* | n.i. | Kumar *et al.*, 2003 |
| Norcepharanone **(3.63)** | *Goniothalamus griffithii* | Root | Zhang *et al.*, 1999 |
| Piperolactam A **(3.64)** | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *F. bracteolatum* | Stem | Lan *et al.*, 2005 |
| | *F. glaucescens* | Leaves | Lo *et al.*, 2000 |
| | *F. oldhamii* | Stem | Chia *et al.*, 2000 |
| | *Oxymitra velutina* | Twig | Achenbach and Hemrich, 1991 |
| Piperolactam C **(3.65)** | *Fissistigma balansae* | Twigs | Chia *et al.*, 2000 |
| | *Uvaria hamiltonii* | Bark | Hasan *et al.*, 2001 |
| Stigmalactam **(3.66)** | *Fissistigma oldhamii* | Twigs | Chia *et al.*, 2000 |
| Velutinam **(3.67)** | *F. oldhamii* | Stem | Chia *et al.*, 2000 |
| | *Goniothalamus griffithii* | Root | Zhang *et al.*, 1999 |
| | *G. tenuifolius* | Bark | Likhitwitayawuid *et al.*, 1997 |
| | *G. velutinus* | Bark | Omar *et al.*, 1992 |

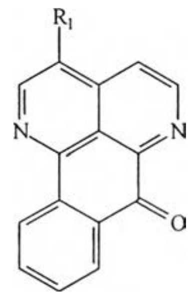



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ | $R_7$ | $R_8$ | $R_9$ |
|---|---|---|---|---|---|---|---|---|---|
| Annolatine **(3.1)** | $OCH_3$ | $OCH_3$ | H | H | OH | $OCH_3$ | H | H | H |
| Artabonatine C **(3.2)** | H | H | H | H | $OCH_3$ | H | H | $OCH_3$ | $OCH_3$ |
| Artabonatine D **(3.3)** | H | H | H | H | $OCH_3$ | H | H | $OCH_3$ | OH |
| Artherospermidine **(3.4)** | H | H | H | H | $-OCH_2O-$ | | $OCH_3$ | H | H |
| Dicentrinone **(3.5)** | H | $OCH_3$ | $OCH_3$ | H | $-OCH_2O-$ | | H | H | H |
| 1,9-Dihydroxy-2,11-dimethoxy-4,5-dihydro-7-oxoaporphine **(3.6)** | H | OH | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H | H |
| Fissicesine **(3.8)** | OH | $OCH_3$ | H | H | $-OCH_2O-$ | | H | H | H |
| 10-Hydroxyliriodenine **(3.9)** | H | H | OH | H | $-OCH_2O-$ | | H | H | H |
| 11-Hydroxy-1,2-methylene-dioxyoxoaporphine **(3.10)** | H | H | H | OH | $-OCH_2O-$ | | H | H | H |
| Kaufumine **(3.11)** | $OCH_3$ | $OCH_3$ | H | H | $-OCH_2O-$ | | $OCH_3$ | H | H |
| Lanuginosine **(3.12)** | H | $OCH_3$ | H | H | $-OCH_2O-$ | | H | H | H |
| Liriodenine **(3.13)** | H | H | H | H | $-OCH_2O-$ | | H | H | H |
| Lysicamine **(3.14)** | H | H | H | H | $OCH_3$ | $OCH_3$ | H | H | H |
| 10-Methoxy-liriodenine **(3.15)** | H | H | $OCH_3$ | H | $-OCH_2O-$ | | H | H | H |
| 11-Methoxy-1,2-methylene-dioxyoxoaporphine **(3.16)** | H | H | H | $OCH_3$ | $-OCH_2O-$ | | H | H | H |
| *O*-Methyl-moschatoline **(3.18)** | H | H | H | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H |
| Oxoanalobine **(3.19)** | H | OH | H | H | $-OCH_2O-$ | | H | H | H |
| Oxoaporphine-3-methoxy-oxoputerine **(3.20)** | H | H | H | $OCH_3$ | $-OCH_2O-$ | | $OCH_3$ | H | H |
| Oxobuxifolina **(3.21)** | H | $OCH_3$ | H | H | $-OCH_2O-$ | | $OCH_3$ | H | H |
| Oxocrebanine **(3.22)** | $OCH_3$ | $OCH_3$ | H | H | $-OCH_2O-$ | | H | H | H |
| Oxoglaucine **(3.23)** | H | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | $OCH_3$ | H | H | H |
| Oxophoebine **(3.24)** | H | $-OCH_2O-$ | | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H |
| Oxostephanine **(3.25)** | $OCH_3$ | H | H | H | $-OCH_2O-$ | | H | H | H |
| Oxoxylopine **(3.26)** | H | $OCH_3$ | H | H | $-OCH_2O-$ | | H | H | H |

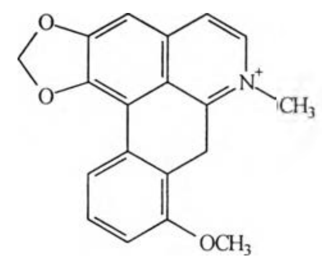
**Figure 5.** Chemical structures of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae



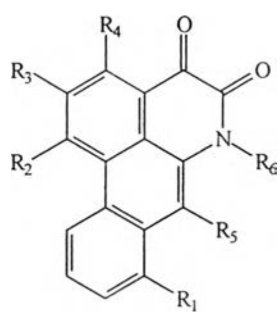

1,2-Dimethoxy-3-hydroxy-5-oxonoraporphine **(3.7)** : $R_1$ = OH
1,2,3-Trimethoxy-5-oxonoraporphine **(3.29)** : $R_1$ = $OCH_3$




3-Methoxysampangine **(3.17)** : $R_1$ = $OCH_3$
Sampangine **(3.27)** : $R_1$ = H

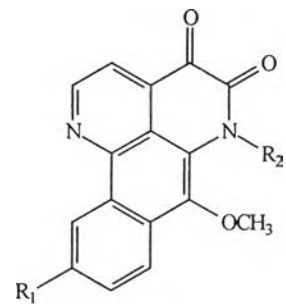



Thailandine **(3.28)**

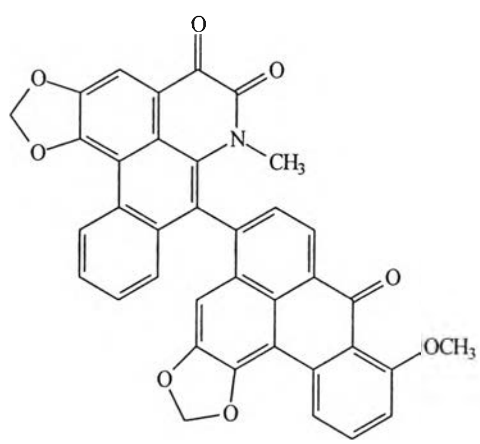



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| Artabotrine **(3.30)** | H | -$OCH_2O$- | | H | H | $OCH_3$ |
| 4,5-Dioxodehydro-asimilobin **(3.31)** | H | $OCH_3$ | OH | H | H | $CH_3$ |
| Griffithidione **(3.32)** | H | $OCH_3$ | $OCH_3$ | H | $CH_3$ | H |
| 3-Methoxy-cepharadione **(3.38)** | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H |
| 8-Methoxy-ouregidione **(3.40)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H |
| N-Methylouregidione**(3.41)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | $CH_3$ |
| Noraristolodione **(3.42)** | H | $OCH_3$ | OH | H | H | H |
| Norcepharadione A **(3.43)** | H | -$OCH_2O$- | | H | H | H |
| Norcepharadione B **(3.44)** | H | $OCH_3$ | $OCH_3$ | H | H | H |
| Ouregidione **(3.45)** | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | H |

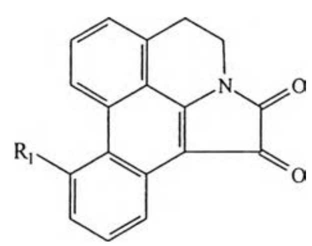
**Figure 5.** Chemical structures of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)



| | $R_1$ | $R_2$ |
|---|---|---|
| Hadranthine A **(3.33)** | $CH_3$ | $CH_3$ |
| Hadranthine B **(3.34)** | H | H |
| Imbiline-1 **(3.35)** | $CH_3$ | H |

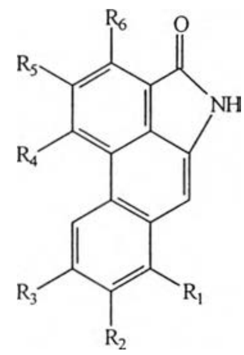


Labeccapolydione **(3.36)**



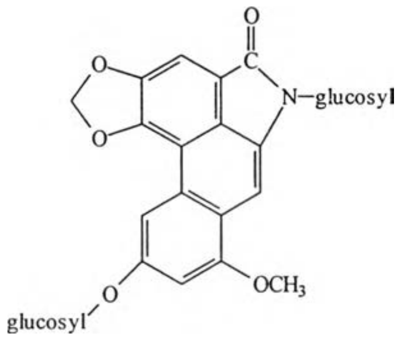
Lettowianthine **(3.37)** : $R_1$ = H
11-Methoxylettowianthine **(3.39)** $R_1$ : $OCH_3$

**Figure 5.** Chemical structures of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

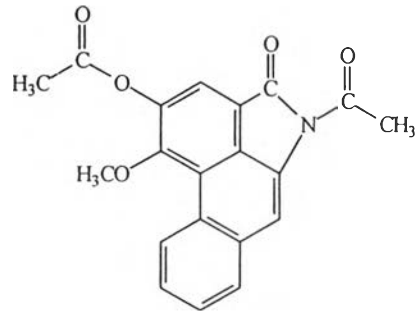


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| 10-Amino-4,8-dihydroxy-3-methoxyphenanthere-1-carboxylic acid lactam **(3.46)** | OH | H | H | OH | $OCH_3$ | H |
| 10-Amino-2,3-dimethoxy-phenanthere-1-carboxylic acid lactam **(3.47)** | H | H | H | H | $OCH_3$ | $OCH_3$ |
| Aristolactam II **(3.48)** | H | H | H | -$OCH_2O$- | | H |
| Aristolactam A Ia **(3.49)** | OH | H | H | $OCH_3$ | OH | H |
| Aristolactam A II **(3.50)** | H | H | H | $OCH_3$ | OH | H |
| Aristolactam A III **(3.51)** | H | H | $OCH_3$ | $OCH_3$ | OH | H |
| Aristolactam A IIIa **(3.52)** | H | H | OH | $OCH_3$ | OH | H |
| Aristolactam B I **(3.53)** | $OCH_3$ | H | H | $OCH_3$ | $OCH_3$ | H |
| Aristolactam B II **(3.54)** | H | H | H | $OCH_3$ | $OCH_3$ | H |
| Aristolactam B III **(3.55)** | H | H | OH | $OCH_3$ | $OCH_3$ | H |
| Aristolactam F II **(3.56)** | H | H | H | $OCH_3$ | OH | $OCH_3$ |
| Enterocarpam II **(3.60)** | $OCH_3$ | H | H | $OCH_3$ | OH | H |
| Goniothalactam **(3.61)** | H | H | OH | $OCH_3$ | $OCH_3$ | H |
| Griffithinam **(3.62)** | $OCH_3$ | H | H | OH | $OCH_3$ | H |
| Norcepharanone **(3.63)** | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| Piperolactam A **(3.64)** | H | H | H | OH | $OCH_3$ | H |
| Piperolactam C **(3.65)** | H | H | H | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| Stigmalactam **(3.66)** | H | H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| Velutinam **(3.67)** | OH | H | H | $OCH_3$ | $OCH_3$ | H |

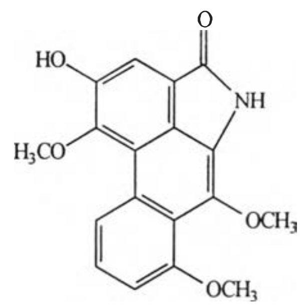
**Figure 5.** Chemical structures of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)




Aristolamide-*N*-hexoside **(3.57)**




*N*-*O*-Diacetylaristolactam A II **(3.58)**




Enterocarpam I **(3.59)**

**Figure 5.** Chemical structures of oxoaporphine, dioxoaporphine and aristolactam alkaloids in the family Annonaceae (continued)

**Lignans**

Lignans are dimers of phenylpropanoid ($C_6$-$C_3$) units linked by the central carbons of their side chains, whereas naturally occuring dimers that connect through position other than this C8-C8′ type of linkage are called neolignans (MacRae and Tower, 1985). These compounds are widely distributed in the plant kingdom. Lignans and neolignans can be found in several annonaceous plants, for examples, *Anaxagorea clavata* (De Diaz, 1997), *Duguetia surinamensis*, *Rollinia exalbida* (Mesquita *et al*., 1988), *Rollinia mucosa* (Chen, Chang and Wu, 1996), and other members of the superorder Magnoliidae, including families of the same order Magnoliales such as Magnoliaceae or Myristicaceae, and other related families e.g. Aristolochiaceae, Lauraceae and Piperaceae.

Lignans can be classified according to the way both phenylpropanoid units are linked into 7 groups, which are 1) Dibenzylbutanes, 2) Dibenzylbutyrolactones, 3) Tetrahydrofuran, 4) Furofurans, 5) Aryltetrahydronaphthalenes (Tetralin lignans), 6) Apolignans and naphthalenes and 7) Dibenzocyclo-octadienes (Ayres and Loike, 1990).

Lignans and neolignans are known to exhibit several remarkable biological activities. Taluamidin, a 2,5-diaryltetrahydrofuran lignan from *Aristolochia arcuata* (family Aristolochiaceae), promoted the outgrowth of neuron in cultured rat cells (Zhai *et al*., 2004). Nectandrin B, which is another lignan of the same subgroup, from *Myristica argentea* (family Myristicaceae), displayed antiaromatase activity (Filleur *et al.*, 2002), whereas three 2,5-diaryltetrahydrofuran lignans, (+)-galbegin, galgravin and (+)-veraguensin, were shown to exhibit platelet-activating factor (PAF) inhibitory activity (Biftu *et al*., 1986). The 2,3-dihydrobenzofuran neolignans dehydroiisoeugenol and 5′-methoxydehydroiisoeugenol were demonstrated as exhibiting antibacterial activity against *Streptococcus mutans* at the concentration 12.5 μg/ml (Hattori *et al*., 1986), antifungal activity (Freixa *et al*., 2001) and inhibiting the growth of insect (Gonzalez-Coloma *et al*., 1994). Licarin A, together with a number of different types of lignans such as (-)-sesamin, (+)-guaiacin, machilin A, (+)-galbelgin and (-)-isoguaiacin, have been found to possess significant neuroprotective activity against glutamate-induced neurotoxicity in primary culture of rat cortical cells at concentrations ranging from 0.1 to 10 μM (Ma, Sung and Kim, 2004).

The distribution in the superorder Magnoliidae of 2,5-diaryltetrahydrofuran lignans, which is a subgroup of the tetrahydrofuran lignans, and 2,3-dihydrobenzofuran neolignans is presented in **Tables 4** and **5**. It should be noted that, currently, xylobuxin **(4.51)** is the only neolignan of its type (2,3-dihydrobenzofuran) reported from a number of the family Annonaceae (Wahl, Roblot and Cave, 1995).

**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae

| Compounds | Sources (family) | Part | References |
|---|---|---|---|
| (7*S*,8*S*)-$\Delta^{8'}$-6-Acetoxy-5′-methoxy-3,4-methylenedioxy-7.O.2′,8.3′-neolignan **(4.1)** | *Mezilaurus itauba* (Lauraceae) | Bark | Yanez, Diaz and Diaz, 1986 |
| (-)-Acuminatin **(4.2)** | *Magnolia kachirachirai* (Magnoliaceae) | Leaves | Ito *et al.*, 1984 |
| (2*R*,3*S*)-7-Allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran **(4.3)** | *Aniba terminalis* (Lauraceae) | Wood | Gottlieb, Silva and Ferreira, 1975 |
| (2*S*,3*S*)-7-Allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran **(4.4)** | *Aniba terminalis* (Lauraceae) | Wood | Gottlieb *et al.*, 1975 |
| (2*S*,3*S*)-5-Allyl-6-hydroxy-2-(3′,4′,5′-trimethoxyphenyl-3-methyl-2,3-dihydrobenzofuran **(4.5)** | *Nectandra miranda* (Lauraceae) | Wood | Aiba *et al.*, 1977 |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-2-(3′-methoxy-4′,5′-methylene-dioxyphenyl)-3-methyl-2,3-dihydrobenzofuran **(4.6)** | *Aniba simulans* (Lauraceae) | Wood | Aiba *et al.*, 1977 |
| | *Licaria armeniaca* (Lauraceae) | Fruits | Barbosa-Filho, Yoshida and Gottlieb, 1987 |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-3-methyl-2-piperonyl-2,3-dihydro-benzofuran **(4.7)** | *Aniba terminalis* (Lauraceae) | Wood | Gottlieb *et al.*, 1975 |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-2-(3′,4′,5′-trimethoxyphenyl)-3-methyl-2,3-dihydrobenzofuran **(4.8)** | *Nectandra Miranda* (Lauraceae) | Wood | Aiba *et al.*, 1977 |
| (7*S*,8*S*)-$\Delta^{8'}$-(3,4),(3′,4′)-Bismethylenedioxy-7.O.2′.8.3′-neolignan **(4.9)** | *Piper capense* (Piperaceae) | Root | Green, Galinis and Wiemer, 1991 |
| Chrysophyllon III-A **(4.10)** | *Licaria chrysophylla* (Lauraceae) | Wood, fruit calyx | Lopes *et al.*, 1986 |

**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (continued)

| Compounds | Sources (Family) | Part | References |
|---|---|---|---|
| Chrysophyllon III-B **(4.11)** | *Licaria chrysophylla* (Lauraceae) | Wood, fruit calyx | Lopes *et al.*, 1986 |
| Conocarpan **(4.12)** | *Caryodaphnopsis baviensis* (Lauraceae) | Fruits | Anh *et al.*, 1997 |
| | *Piper fulvescens* (Piperaceae) | Leaves | Freixa *et al.*, 2001 |
| Decurrenal **(4.13)** | *P. aequale* (Piperaceae) | Aerial parts | Maxwell *et al.*, 1999 |
| Dihydrocarinatidin **(4.14)** | *Virola carinata* (Myristicaceae) | Bark, fruits | Kawanishi, Uhara and Hashimoto, 1983; Cavalcante, Yoshida and Gottlieb, 1985 |
| Dihydrocarinatin **(4.15)** | *Virola pavonis* (Myristicaceae) | Seed coat | Marques, Yoshida and Gottlieb, 1992 |
| Dihydrocarinatinol **(4.16)** | *V. carinata* (Myristicaceae) | Fruits | Cavalcante *et al.*, 1985 |
| (2*R*,3*R*)-2,3-Dihydro-2-(4-hydroxyphenyl)-5-methoxy-3-methyl-7-propenylbenzofuran **(4.17)** | *Piper aequale* (Piperaceae) | Aerial parts | Maxwell *et al.*, 1999 |
| (2*S*,3*S*)-2,3-Dihydro-2-(4-hydroxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran **(4.18)** | *P. aequale* (Piperaceae) | Aerial parts | Maxwell *et al.*, 1999 |
| (2*R*,3*R*)-2,3-Dihydro-2-(4-hydroxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran **(4.19)** | *P. aequale* (Piperaceae) | Aerial parts | Maxwell *et al.*, 1999 |
| (2*S*,3*S*)-2,3-Dihydro-7-methoxy-3-methyl-2-(3,4-dimethoxyphenyl)-5-*trans*-(1-propenyl)-benzofuran **(4.20)** | *Machilus japonica* (Lauraceae) | Leaves | Gonzalez-Coloma *et al.*, 1994 |

**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (Continued)

| Compounds | Sources (Family) | Part | References |
|---|---|---|---|
| (7*S*,8*S*)-$\Delta^{8'}$-2′,6′-Dimethoxy-3,4-methylenedioxy-7.O.3′,8.4′,1′.O.7′-neolignan **(4.21)** | *Ocotea catharrinensis* (Lauraceae) | Stem, leaves | Ishige *et al*., 1991 |
| | *O. veraguensis* (Lauraceae) | Bark | Khan, Gray and Waterman, 1987 |
| Eupomatenoid-8 **(4.22)** | *Virola oleifera* (Myristicaceae) | Leaves | Fernandes, Barata and Ferri, 1993 |
| Fragransol-A **(4.23)** | *Myristica fragrans* (Myristicaceae) | Aril | Hada *et al*., 1988 |
| Fragransol-B **(4.24)** | *M. fragrans* (Myristicaceae) | Aril | Hada *et al*., 1988 |
| (7*S*,8*S*)-$\Delta^{8'}$-6′-Hydroxy-5′-methoxy-3,4-methylenedioxy-7.O.2′-8.3′-neolignan **(4.25)** | *Mezilaurus itauba* (Lauraceae) | Bark | Yanez *et al*., 1986 |
| (7*S*,8*S*)-$\Delta^{8'}$-4-Hydroxy-3-methoxy-3′,4′-methylenedioxy-7.O.2′-8.3′-neolignan **(4.26)** | *Piper capense* (Piperaceae) | Root | Green *et al*., 1991 |
| (7*S*,8*S*)-4-Hydroxy-3,3′-dimethoxy-7′-oxo-8,5′,7.O.4′-8′,9′-bisnorneolignan **(4.27)** | *Ocotea porosa* (Lauraceae) | Bark, leaves | David, Yoshida and Gottlieb, 1994 |
| (7*S*,8*R*)-4-Hydroxy-4′,7-epoxy-8,3′-neolignan-7′[*E*]-ene **(4.28)** | *Piper regnellii* (Piperaceae) | Root | Benevides, Sartorelli and Kato, 1999 |
| (7*S*,8*R*)-4-Hydroxy-8′,9′-dinor-4′,7-epoxy-8,3′-neolignan-7′-aldehyde **(4.29)** | *P. aequale* (Piperaceae) | Aerial parts | Maxwell *et al*., 1999 |
| | *P. regnellii* (Piperaceae) | Root | Benevides *et al*., 1999 |
| Kachirachirol-B **(4.30)** | *Magnolia kachirachirai* (Magnoliaceae) | Leaves | Ito *et al*., 1984 |

**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (Continued)

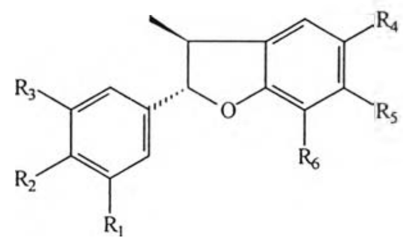
| Compounds | Sources (Family) | Part | References |
|---|---|---|---|
| Licarin A (**4.31**) | *Aniba sp.* (Lauraceae) | Wood | Rossi, Yoshida and Maia, 1997 |
| | *Aristolochia pubescens* (Aristolochiaceae) | Stem, root | Nascimento and Lopes, 1999 |
| | *Licaria aritu* (Lauraceae) | Wood | Aiba, Correa and Gottlieb, 1973 |
| | *Machilus japonica* (Lauraceae) | Leaves | Gonzales-Coloma *et al.*, 1994 |
| | *M. thunbergii* (Lauraceae) | Bark | Shimomura, Sashida and Oohara, 1987; Ma, Sung and Kim, 2004a |
| | *Magnolia kachirachirai* (Magnoliaceae) | Leaves | Ito *et al.*, 1984 |
| | *Myristica argentea* (Myristicaceae) | Aril | Filleur *et al.*, 2002 |
| | *Nectandra rigida* (Lauraceae) | Leaves, stem | Quesne, Larranhondo and Raffauf, 1980 |
| | *Ocotea porosa* (Lauraceae) | Bark, leaves | David *et al.*, 1994 |
| | *Urbanodendron verrucosum* (Lauraceae) | Wood | Dias, Giesbrecht and Gottlieb, 1982 |
| Licarin B (**4.32**) | *Licaria aritu* (Lauraceae) | Wood | Aiba *et al.*, 1973 |
| | *Machilus thunbergii* (Lauraceae) | Bark | Shimomura *et al.*, 1987 |
| | *Magnolia kachirachirai* (Magnoliaceae) | Leaves | Ito *et al.*, 1984 |
| | *Myristica argentea* (Myristicaceae) | Aril | Filleur *et al.*, 2002 |
| | *Ocotea porosa* (Lauraceae) | Wood | Dias, Yoshida and Gottlieb, 1986; David *et al.*, 1994 |
| Licarin C (**4.33**) | *Nectandra miranda* (Lauraceae) | Wood | Aiba *et al.*, 1977 |
| Licarin D (**4.34**) | *Urbanodendron verrucosum* (Lauraceae) | Wood | Dias *et al.*, 1982 |

**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (Continued)

| Compounds | Sources (Family) | Part | References |
|---|---|---|---|
| Licarin E **(4.35)** | *Nectandra glabrescens* (Lauraceae) | Fruits | Barbosa-Filho *et al.*, 1989 |
| Liliflol A **(4.36)** | *Magnolia lilifolia* (Magnoliaceae) | Leaves | Iida and Ito, 1983 |
| Liliflol B **(4.37)** | *M. lilifolia* (Magnoliaceae) | Leaves | Iida and Ito, 1983 |
| Machilin B **(4.38)** | *Machilus thunbergii* (Lauraceae) | Bark | Shimomura *et al.*, 1987 |
| (7*R*,8*S*)-3-Methoxy-4-hydroxy-4′,7-epoxy-8,3′-neolignan-7′-ene **(4.39)** | *Piper regnellii* (Piperaceae) | Root | Benevides *et al.*, 1999 |
| (7*S*,8*S*)-$\Delta^{8'}$-6′-Methoxy-3,4-methylenedioxy-7.O.3′, 8.4′,1′.O.7′-neolignan **(4.40)** | *Mezilaurus itauba* (Lauraceae) | Bark | Yanez *et al.*, 1986 |
| (2*R*,3*R*)-7-Methoxy-3-methyl-5-propenyl-2-veratryl-2,3-dihydrobenzofuran **(4.41)** | *Aniba sp.* (Lauraceae) | Bark | Fernandes, Gottlieb and Maia, 1976 |
| | *Nectandra miranda* (Lauraceae) | Wood | Aiba *et al.*, 1977 |
| (7*R*,8*S*)-3,4-Methylene-dioxyphenyl-4′,7-epoxy-8,3′-neolignan-7′-ene (Regnelline) **(4.42)** | *Piper regnellii* (Piperaceae) | Roots | Benevides *et al.*, 1999 |
| Methyl-(7*R*,8*R*)-4-hydroxy-8′,9′-dinor-4′,7-epoxy-8,3′-neolignan-7′-ate **(4.43)** | *P. regnellii* (Piperaceae) | Roots | Benevides *et al.*, 1999 |
| Methyl-(7*R*,8*R*)-4-hydroxy-8′,9′-dinor-4′,7-epoxy-8,3′-neolignan-7′-aldehyde **(4.44)** | *P. regnellii* (Piperaceae) | Roots | Benevides *et al.*, 1999 |
| Schmiditin **(4.45)** | *P. schmidtii* (Piperaceae) | Aerial part | Joshi, Garg and Bhakuni, 1990 |
| (7*S*,8*S*)-3′-Methoxy-3,4-methylenedioxy-7′-oxo-8.5′,7.O.4′-8′,9′-bisnorneolignan **(4.46)** | *Ocotea porosa* (Lauraceae) | Bark, leaves | David *et al.*, 1994 |

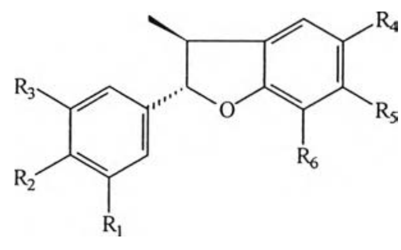
**Table 4**. Distribution of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (Continued)

| Compounds | Sources (Family) | Part | References |
|---|---|---|---|
| Obovatinal **(4.47)** | *Persea obovatifolia* (Lauraceae) | Leaves | Tsai *et al*., 1996 |
| Obovatifol **(4.48)** | *P. obovatifolia* (Lauraceae) | Leaves | Tsai, Hsieh and Duh, 1998 |
| Perseal C **(4.49)** | *P. obovatifolia* (Lauraceae) | Leaves | Tsai *et al*., 1998 |
| (7*S*,8*S*)-$\Delta^{1',3',5',8'}$-5,3′,5′-Trimethoxy-3,4-methylene dioxy-8.1′,7.O.6′,4′.O.7′-neolignan **(4.50)** | *Ocotea catharrinensis* (Lauraceae) | Stem, leaves | Ishige *et al*., 1991 |
| Xylobuxin **(4.51)** | *Xylopia buxifolia* (Annonaceae) | Bark | Wahl, Roblot and Cave, 1995 |



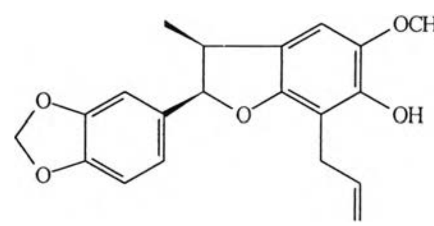

| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| (7*S*,8*S*)-$\Delta^{8'}$-6-Acetoxy-5′-methoxy-3,4-methylenedioxy-7.O.2′,8.3′-neolignan **(4.1)** | H | -$OCH_2O$- | | $OCH_3$ | OAc | allyl |
| (-)-Acuminatin **(4.2)** | H | $OCH_3$ | $OCH_3$ | propenyl | H | $OCH_3$ |
| (2*S*,3*S*)-7-Allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran **(4.4)** | H | -$OCH_2O$- | | $OCH_3$ | OH | allyl |
| (2*S*,3*S*)-5-Allyl-6-hydroxy-2-(3′,4′,5′-trimethoxyphenyl-3-methyl-2,3-dihydrobenzofuran **(4.5)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | allyl | OH | H |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-2-(3′-methoxy-4′,5′-methylenedioxyphenyl)-3-methyl-2,3-dihydrobenzofuran **(4.6)** | $OCH_3$ | -$OCH_2O$- | | $OCH_3$ | *O*-allyl | H |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran **(4.7)** | H | -$OCH_2O$- | | $OCH_3$ | *O*-allyl | H |
| (2*S*,3*S*)-6-*O*-Allyl-5-methoxy-2-(3′,4′,5′-trimethoxyphenyl)-3-methyl-2,3-dihydrobenzofuran **(4.8)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | *O*-allyl | H |
| Conocarpan **(4.12)** | H | OH | H | propenyl | H | H |
| Decurrenal **(4.13)** | $OCH_3$ | OH | H | allyl | H | $OCH_3$ |
| Dihydrocarinatidin **(4.14)** | H | $OCH_3$ | $OCH_3$ | allyl | H | $OCH_3$ |
| (2*S*,3*S*)-2,3-Dihydro-2-(4-hydroxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran **(4.18)** | H | OH | H | propenyl | H | H |
| (7*S*,8*S*)-$\Delta^{8'}$-2′,6′-Dimethoxy-3,4-methylenedioxy-7.O.3′,8.4′,1′.O.7′-neolignan **(4.21)** | H | -$OCH_2O$- | | $OCH_3$ | *O*-allyl | $OCH_3$ |

**Figure 6.** Chemical structures of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae

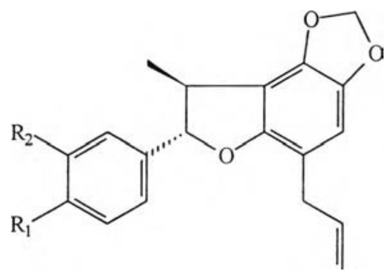



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| Eupomatenoid-8 **(4.22)** | H | -$OCH_2O$- | | propenyl | H | $OCH_3$ |
| (7*S*,8*S*)-$\Delta^{8'}$-6'-Hydroxy-5'methoxy-3,4-methylenedioxy-7.O.2'-8.3'-neolignan **(4.25)** | H | -$OCH_2O$- | | $OCH_3$ | OH | allyl |
| (7*S*,8*S*)-4-Hydroxy-3,3'-dimethoxy-7'-oxo-8,5',7.O.4'-8',9'-bisnorneolignan **(4.27)** | H | OH | $OCH_3$ | CHO | H | $OCH_3$ |
| Kachirachirol-B **(4.30)** | H | OH | OH | propenyl | H | $OCH_3$ |
| Licarin A **(4.31)** | H | OH | $OCH_3$ | propenyl | H | $OCH_3$ |
| Licarin B **(4.32)** | H | -$OCH_2O$- | | propenyl | H | $OCH_3$ |
| Liliflol A **(4.36)** | H | -$OCH_2O$- | | allyl | OH | H |
| Liliflol B **(4.37)** | H | $OCH_3$ | $OCH_3$ | allyl | OH | H |
| Machilin B **(4.38)** | H | -$OCH_2O$- | | propanoyl | H | $OCH_3$ |
| (7*S*,8*S*)-$\Delta^{8'}$-6'-Methoxy-3,4-methylenedioxy-7.O.3'-8.4',1'.O.7'-neolignan **(4.40)** | H | -$OCH_2O$- | | $OCH_3$ | *O*-allyl | H |
| (7*S*,8*S*)-3'-Methoxy-3,4-methylenedioxy-7'-oxo-8.5',7.O.4'-8',9'-bisnorneolignan **(4.46)** | H | -$OCH_2O$- | | propenyl | H | $OCH_3$ |
| (7*S*,8*S*)-$\Delta^{1',3',5',8'}$-5,3',5'-Trimethoxy-3,4-methylenedioxy-8.1',7.O.6',4'.O.7'-neolignan **(4.50)** | $OCH_3$ | -$OCH_2O$- | | $OCH_3$ | *O*-allyl | $OCH_3$ |

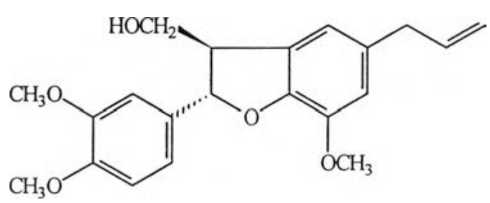
**Figure 6.** Chemical structures of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (continued)



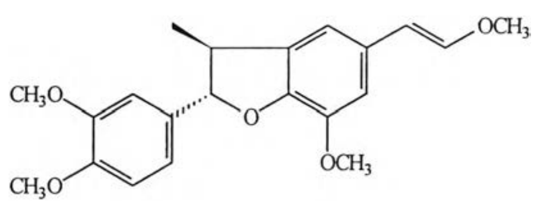
(2*R*,3*S*)-7-Allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran **(4.3)**



| | $R_1$ | $R_2$ |
|---|---|---|
| (7*S*,8*S*)-$\Delta^{8'}$-(3,4),(3',4')-Bismethylene dioxy-7.O.2'.8.3'-neolignan **(4.9)** | -$OCH_2O$- | |
| (7*S*,8*S*)-$\Delta^{8'}$-4-Hydroxy-3-methoxy-3',4'-methylenedioxy-7.O.2'-8.3'-neolignan **(4.26)** | OH | $OCH_3$ |

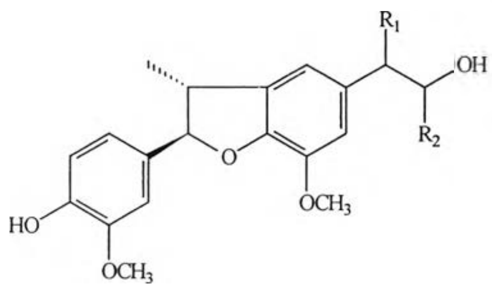


Dihydrocarinatin **(4.15)**

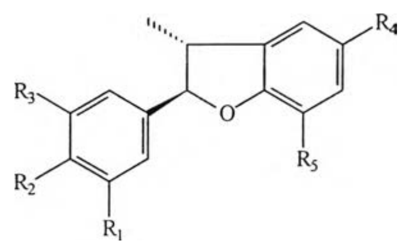


(2*S*,3*S*)-2,3-Dihydro-7-methoxy-3-methyl-2-(3,4-dimethoxyphenyl)-5-*trans*-(1-propenyl)-benzofuran **(4.20)**

**Figure 6.** Chemical structures of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (continued)

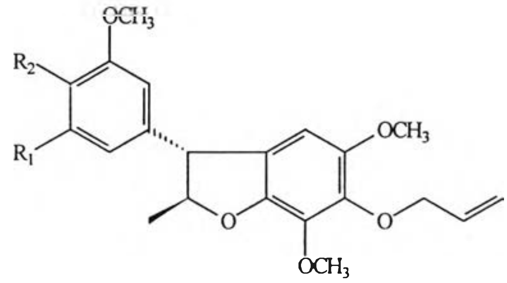



| | $R_1$ | $R_2$ |
|---|---|---|
| Fragransol-A **(4.23)** | $OCH_3$ | $CH_3$ |
| Fragransol-B **(4.24)** | H | H |

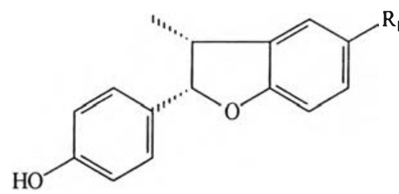



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ |
|---|---|---|---|---|---|
| Decurrenal **(4.13)** | H | OH | H | CHO | H |
| (2*R*,3*R*)-2,3-Dihydro-2-(4-hydroxyphenyl)-5-methoxy-3-methyl-7-propenylbenzofuran **(4.17)** | H | OH | H | $OCH_3$ | allyl |
| (2*R*,3*R*)-2,3-Dihydro-2-(4-hydroxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran **(4.19)** | H | OH | $OCH_3$ | propenyl | H |
| Licarin C **(4.33)** | $OCH_3$ | $OCH_3$ | $OCH_3$ | propenyl | $OCH_3$ |
| Licarin D **(4.34)** | $OCH_3$ | $OCH_3$ | H | propenyl | $OCH_3$ |
| Licarin E **(4.35)** | H | $-OCH_2O-$ | | propenyl | $OCH_3$ |
| (7*R*,8*S*)-3-Methoxy-4-hydroxy-4′,7-epoxy-8,3′-neolignan-7′-ene **(4.39)** | H | OH | $OCH_3$ | propenyl | H |
| (2*R*,3*R*)-7-Methoxy-3-methyl-5-propenyl-2-veratryl-2,3-dihydrobenzofuran **(4.41)** | H | $OCH_3$ | $OCH_3$ | propenyl | $OCH_3$ |
| (7*R*,8*S*)-3,4-Methylenedioxyphenyl-4′,7-epoxy-8,3′-neolignan-7′-ene (Regnelline) **(4.42)** | H | $-OCH_2O-$ | | propenyl | H |
| Methyl-(7*R*,8*R*)-4-hydroxy-8′,9′-dinor-4′,7-epoxy-8,3′-neolignan-7′-aldehyde **(4.44)** | H | OH | H | CHO | H |
| Obovatinal **(4.47)** | OH | $OCH_3$ | $OCH_3$ | CHO | $OCH_3$ |
| Obovatifol **(4.48)** | OH | OH | $OCH_3$ | propenyl | $OCH_3$ |
| Perseal C **(4.49)** | H | $-OCH_2O-$ | | CHO | $OCH_3$ |

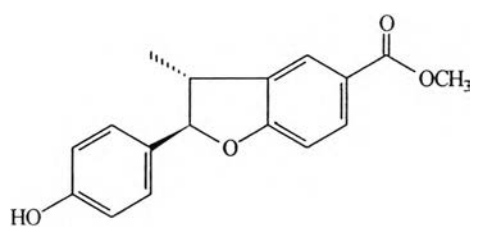
**Figure 6.** Chemical structures of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (continued)



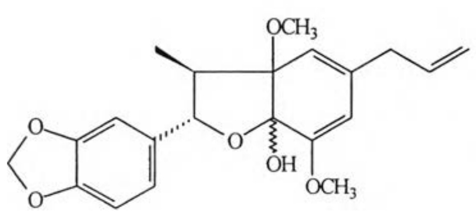
| | $R_1$ | $R_2$ |
|---|---|---|
| Chrysophyllon III-A **(4.10)** | $-OCH_2O-$ | |
| Chrysophyllon III-B **(4.11)** | $OCH_3$ | $OCH_3$ |



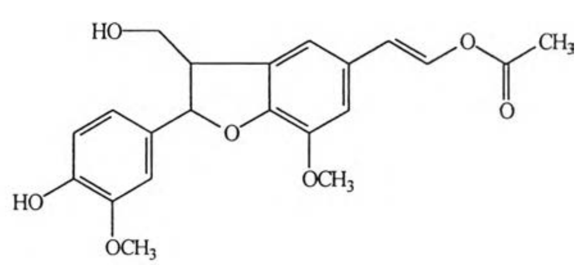
| | $R_1$ |
|---|---|
| (7*S*,8*R*)-4-Hydroxy-4',7-epoxy-8,3'-neolignan-7'[*E*]-ene **(4.28)** | propenyl |
| (7*S*,8*R*)-4-Hydroxy-8',9'-dinor-4',7-epoxy-8,3'-neolignan-7'-aldehyde **(4.29)** | CHO |



Methyl-(7*R*,8*R*)-4-hydroxy-8',9'-dinor-4',7-epoxy-8,3'-neolignan-7'-ate **(4.43)**



Schmiditin **(4.45)**



Xylobuxin **(4.51)**

**Figure 6.** Chemical structures of 2,3-dihydrobenzofuran neolignans in the superorder Magnoliidae (continued)

**Table 5.** Distribution of tetrahydrofuran lignans in the superorder Magnoliidae

| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| (+)-Aristolignin (**5.1**) | *Aniba sp.* | Lauraceae | Wood | Rossi *et al.*, 1997 |
| | *Virola oleifera* | Myristicaceae | Leaves | Fernandes *et al.*, 1993 |
| | *V. surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Austrobailignan-7 (**5.2**) | *Aristolochia chilensis* | Aristolochiaceae | Root | Urzua, Freyer and Shamma, 1987 |
| | *Urbanodendron verrucosum* | Lauraceae | Wood | Dias *et al.*, 1982 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Calopiptin (**5.3**) | *Aristolochia chilensis* | Aristolochiaceae | Root | Urzua *et al.*, 1987 |
| | *Magnolia acuminata* | Magnoliaceae | Root bark | Doskotch and Flom, 1972 |
| | *Piper schmidtii* | Piperaceae | Leaves | Tyagi *et al.*, 1993 |
| | *Urbanodendron verrucosum* | Lauraceae | Wood | Dias *et al.*, 1982 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| (2*S*,3*S*,4*R*,5*R*)-2-(3,4-Dimethoxyphenyl)-3,4-dimethyl-5-piperonyl-tetrahydrofuran (**5.4**) | *Machilus japonica* | Lauraceae | Leaves | Gonzalez-Coloma *et al.*, 1994 |
| (8*R*,8'*R*)-Dimethyl-(7*S*,7'*R*)-bis(3,4-methylenedioxy-phenyl)tetrahydrofuran (**5.5**) | *Myristica dactyloides* | Myristicaceae | Bark | Herath and Priyadarshani, 1996 |
| Fragransins A2 (**5.6**) | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Fragransin-D1 (**5.7**) | *Myristica fragrans* | Myristicaceae | Aril | Hada *et al.*, 1988 |
| Fragransin-D2 (**5.8**) | *M. fragrans* | Myristicaceae | Aril | Hada *et al.*, 1988 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Fragransin-D3 (**5.9**) | *Myristica fragrans* | Myristicaceae | Aril | Hada *et al.*, 1988 |
| Fragransin-E1 (**5.10**) | *M. fragrans* | Myristicaceae | Aril | Hada *et al.*, 1988 |

**Table 5**. Distribution of tetrahydrofuran lignans in the superorder Magnoliidae (continued)

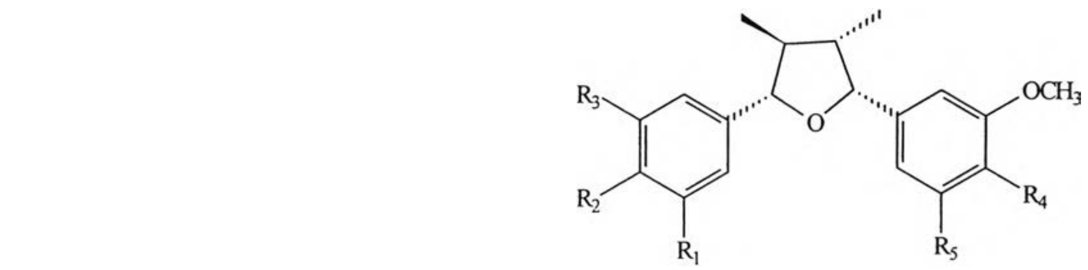
| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| (-)-Galbacin (**5.11**) | *Aristolochia arcuata* | Aristolochiaceae | Root, leaves | Watanabe and Lopez, 1995 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| (+)-Galbacin (**5.12**) | *V. oleifera* | Myristicaceae | Leaves | Fernandes *et al.*, 1993 |
| | *V. surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| (+)-Galbelgin (**5.13**) | *Magnolia kachirachirai* | Magnoliaceae | Leaves | Ito *et al.*, 1984 |
| | *Machilus thunbergii* | Lauraceae | Bark | Ma *et al.*, 2004a |
| (-)-Galbelgin (**5.14**) | *Piper attenuatum* | Piperaceae | Leaves | Sumathykutty and Rao, 1991 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Galgravin (**5.15**) | *Magnolia acuminata* | Magnoliaceae | Root bark | Doskotch and Flom, 1972 |
| | *Virola surinamensis* | Myristicaceae | Seed, pericarp | Blumenthal, Silva and Yoshida, 1997; Lopes *et al.*, 1998 |
| (-)-Grandisin (**5.16**) | *Litsea grandis* | Lauraceae | Bark | Holloway and Scheinmann, 1974 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| (7*S*,8*S*,7′*S*,8′*S*)-4′-Hydroxy-3′-methoxy-3,4-methylene dioxy-8.8′,7.O.7′-neolignan-Δ:1,3,5,1′,3′,5′ (**5.17**) | *V. surinamensis* | Myristicaceae | Seed | Blumenthal *et al.*, 1997 |
| (7*S*,8*S*,7′*R*,8′*R*)-3,3′,4,4′,5,5′-Hexamethoxy-7.O.7′,8.8′-lignan (**5.18**) | *Aristolochia birostris* | Aristolochiaceae | Root | Conserva, Silva, and Filho 1990 |

**Table 5.** Distribution of tetrahydrofuran lignans in the superorder Magnoliidae (continued)

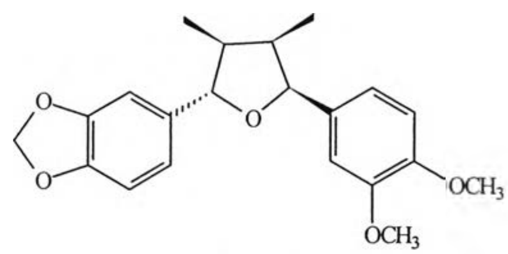
| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| Malabaricanol-A **(5.19)** | *Myristica dactyloides* | Myristicaceae | Bark | Herath and Priyadarshini, 1997 |
| | *M. fragrans* | Myristicaceae | Aril | Purushothaman, Sarada and Connolly, 1984 |
| Machilin F **(5.20)** | *Machilus thunbergii* | Lauraceae | Bark | Shimomura, Sashida and Oohara, 1988 |
| Machilin G **(5.21)** | *M. thunbergii* | Lauraceae | Bark | Shimomura *et al.*, 1988 |
| | *Piper schmidtii* | Piperaceae | Leaves | Tyagi *et al.*, 1993 |
| Machilin H **(5.22)** | *Machilus thunbergii* | Lauraceae | Bark | Shimomura *et al.*, 1988 |
| Machilin I **(5.23)** | *M. thunbergii* | Lauraceae | Bark | Shimomura *et al.*, 1988 |
| | *Piper clarkii* | Piperaceae | Stem, leaves | Prasad *et al.*, 1995 |
| (-)-Machilusin **(5.24)** | *Machilus japonica* | Lauraceae | Leaves | Gonzalez-Coloma *et al.*, 1994 |
| (+)-Nectandrin-A **(5.25)** | *M. thunbergii* | Lauraceae | Bark | Shimomura *et al.*, 1988 |
| | *Nectandra rigida* | Lauraceae | Leaves, stem | Quesne *et al.*, 1980 |
| Nectandrin-B **(5.26)** | *Machilus thunbergii* | Lauraceae | Bark | Shimomura *et al.*, 1988 |
| | *Myristica argentea* | Myristicaceae | Aril | Filleur *et al.*, 2002 |
| | *M. dactyloides* | Myristicaceae | Bark | Herath and Priyadarshini, 1997 |
| | *Nectandra rigida* | Lauraceae | Leaves, stem | Quesne *et al.*, 1980 |
| | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |

**Table 5**. Distribution of tetrahydrofuran lignans in the superorder Magnoliidae (continued)

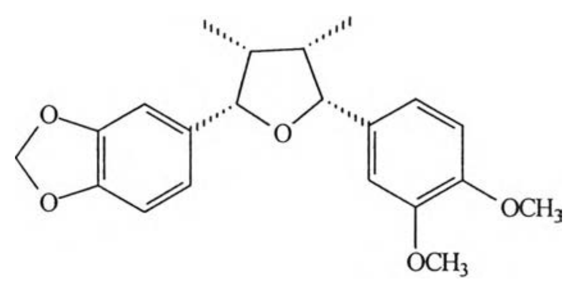
| Compounds | Sources | Family | Part | References |
|---|---|---|---|---|
| (7*S*,8*S*,7′*S*,8′*S*)-3,4,5,3′,4′-Pentamethoxy-7,7′-epoxylignan **(5.27)** | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Talaumidin **(5.28)** | *Aristolochia arcuata* | Aristolochiaceae | Root | Zhai *et al.*, 2004 |
| (7*S*,8*S*,7′*S*,8′*S*)-3,4,5-Trimethoxy-3′,4′-methylenedioxy-7,7′-epoxylignan **(5.29)** | *Virola surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Veraguensin **(5.30)** | *Magnolia acuminata* | Magnoliaceae | Root bark | Doskotch and Flom, 1972 |
| | *M. liliflora* | Magnoliaceae | Leaves | Iida and Ito, 1983 |
| | *Nectandra puberula* | Lauraceae | Wood | Moro *et al.*, 1987 |
| | *Ocotea veraguensis* | Lauraceae | Bark | Khan *et al.*, 1987 |
| | *Virola surinamensis* | Myristicaceae | Leaves, pericarp | Lopes *et al.*, 1996; 1998 |
| (+)-Verrucosin **(5.31)** | *V. surinamensis* | Myristicaceae | Leaves | Lopes *et al.*, 1996 |
| Zuionin-B **(5.32)** | *Aristolochia arcuta* | Aristolochiaceae | Root, leaves | Watanabe and Lopez, 1995 |
| | *Myristica dactyloides* | Myristicaceae | Bark | Herath and Priyadarshini, 1996 |
| (-)-Zuionin A **(5.33)** | *Piper schmidtii* | Piperaceae | Leaves | Tyagi *et al.*, 1993 |



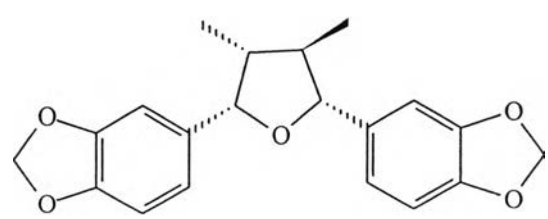

| | R1 | R2 | R3 | R4 | R5 |
|---|---|---|---|---|---|
| (+)-Aristolignin **(5.1)** | : H | OH | $OCH_3$ | $OCH_3$ | H |
| Austrobailignan-7 **(5.2)** | : H | -$OCH_2O$- | | OH | H |
| Calopiptin **(5.3)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| Fragransin-D3 **(5.9)** | : H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| (+)-Verrucosin **(5.31)** | : H | OH | $OCH_3$ | OH | H |
| Veraguensin **(5.30)** | : H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |




(-)-Machilusin **(5.24)**

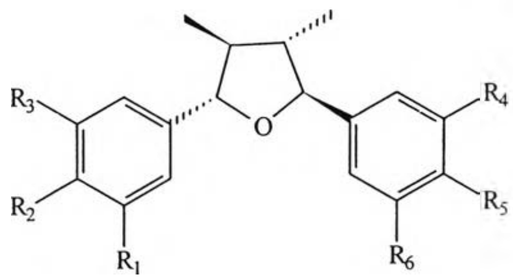



(2*S*,3*S*,4*R*,5*R*)-2-(3,4-Dimethoxyphenyl-3,4-dimethyl-5-piperonyl-tetrahydrofuran **(5.5)**

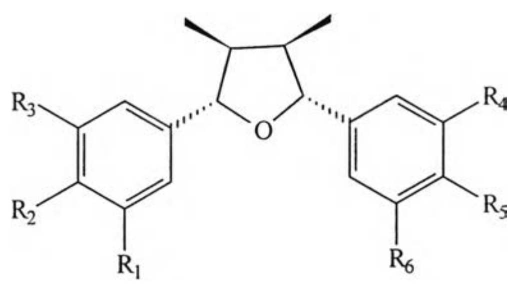



(8*R*,8′*R*)-Dimethyl-(7*S*,7′*R*)-bis(3,4-methylenedioxyphenyl) tetrahydrofuran **(5.5)**

**Figure 7.** Chemical structures of tetrahydrofuran lignans in the superorder Magnoliidae

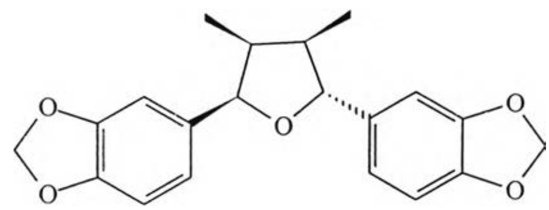


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| Fragransins A2 **(5.6)** | : H | OH | $OCH_3$ | H | $OCH_3$ | OH |
| Fragransin-D2 **(5.8)** | : H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| (-)-Galbacin **(5.11)** | : H | -$OCH_2O$- | | -$OCH_2O$- | | H |
| (-)-Galbelgin **(5.14)** | : H | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| (-)-Grandisin **(5.16)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| (7*S*,8*S*,7′*S*,8′*S*)-4′-Hydroxy-3′-methoxy-3,4-methylenedioxy-8.8′,7.*O*.7′-neolignan-Δ:1,3,5,1′,3′,5′ **(5.17)** | : H | -$OCH_2O$- | | $OCH_3$ | OH | H |
| (7*S*,8*S*,7′*S*,8′*S*)-3,4,5,3′4′-Pentamethoxy-7,7′-epoxylignan **(5.27)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| Talaumidin **(5.28)** | : H | $OCH_3$ | $OCH_3$ | OH | $OCH_3$ | H |
| (7*S*,8*S*,7′*S*,8′*S*)-3,4,5,-Trimethoxy-3′4′-methylenedioxy-7,7′-epoxylignan **(5.29)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | -$OCH_2O$- | | H |

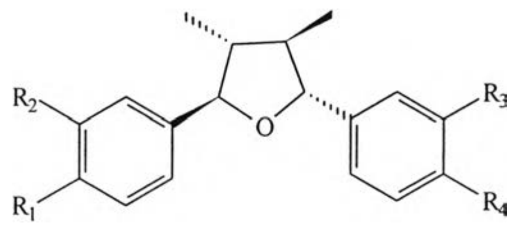


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ |
|---|---|---|---|---|---|---|
| Fragransin- D1 **(5.7)** | : H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| Fragransin-E1 **(5.10)** | : H | -$OCH_2O$- | | OH | OH | H |
| Galgravin **(5.15)** | : H | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| (7*S*,8*S*,7′*R*,8′*R*)-3,3′,4,4′,5,5′-Hexamethoxy-7.O.7′,8.8′-lignan **(5.18)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| Malabaricanol-A **(5.19)** | : H | OH | $OCH_3$ | $OCH_3$ | OH | $OCH_3$ |
| Machilin F **(5.20)** | : H | -$OCH_2O$- | | $OCH_3$ | OH | H |
| Machilin H **(5.22)** | : H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| Machilin G **(5.21)** | : H | -$OCH_2O$- | | $OCH_3$ | $OCH_3$ | H |
| Machilin I **(5.23)** | : H | OH | $OCH_3$ | $OCH_3$ | OH | $OCH_3$ |
| (+)-Nectandrin-A **(5.25)** | : H | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | H |
| Nectandrin-B **(5.26)** | : H | OH | $OCH_3$ | $OCH_3$ | OH | H |
| Zuionin-B **(5.32)** | : H | -$OCH_2O$- | | -$OCH_2O$- | | H |

**Figure 7.** Chemical structures of tetrahydrofuran lignans in the superorder Magnoliidae (continued)



(-)-Zuionin A **(5.33)**



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| (+)-Galbacin **(5.12)** | : -$OCH_2O$- | | -$OCH_2O$- | |
| (+)-Galbelgin **(5.13)** | : $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ |

**Figure 7.** Chemical structures of tetrahydrofuran lignans in the superorder Magnoliidae (continued)